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THE CLASSIFICATION OF PULMONARY TUBERCULOSIS

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From the Municipal Sanatorium, Otisville, New York, in the service of the Bureau of Hospitals, Department of Health of the City of New York

The classification of pulmonary phthisis has occupied the attention of that part of the medical profession interested in tuberculosis since ancient times. The writer purposes to give a general resume of the most important classifications to date and to call attention to the rearrangement of the National Association classification of pulmonary tuberculosis as adopted by the American Sanatorium Association at the twelfth mid-winter meeting on December 7 of last year. This rearrangement was worked out at Otisville by the writer in 1910. Most of the historical data which I present was obtained from Meissen's very complete article[1] on the classification of tuberculosis, Turban's "Diagnosis of Tuberculosis of the Lung,"[2] and Lawrason Brown's article,[3] "The Classification of Pulmonary Tuberculosis."

To quote Meissen:

> The form and course of the disease are dependent on the following:
>
> a. Severity of infection: (1) virulence of the germ, (2) dose of infection, (3) channels of infection.
>
> b. The resistance of the organism, which varies with the special constitutional factors in a given case.
>
> The variegated picture which the reciprocal action of the above two factors (a) and (b) induce is necessarily great. However, it is still possible to form clinical groups, although such groups are necessarily not so sharply defined as for instance one finds in a botanical classification.

Very early writers classified tuberculosis into acute and chronic or protracted forms. This is of some value based as it is on a symptomatic, pathological basis. The chronic form was separated into groups according to the course of the disease: active and stationary, progressive

[1] Handbuch der Tuberculose, Band I, p. 743. Published by Barth, Leipzig, 1914.

[2] Diagnosis of Tuberculosis of the Lung. Turban. Edition 1906, pp. 42–49.

[3] The Classification of Pulmonary Tuberculosis, Lawrason Brown, Journal of the American Medical Association, January 30, 1909.

and regressive, intermittent and remittent, etc. Another early classification was based on the origin of the disorder: congenital or hereditary and acquired. By hereditary is understood a predisposition, the result of body conformation or any structural development of the body which favors the development of the disease. In the acquired form such conditions are absent. Another classification is based on the presence of a dyscrasia or diseased condition which favors the development of tuberculosis, such as tuberculosis of the diabetic, arthritic, alcoholic, syphilitic, hysteric, etc. For example, tuberculosis of the gouty has a slow, favorable course, while in the diabetic the disease is nearly always unfavorable and rapidly progressive.

Cases were also classified as masked (*larvierte*), latent or manifest tuberculosis; also according to the initial symptoms, "phthisis haemoptysis," "phthisis pleuritis," "phthisis bronchitis," "phthisis following anaemia, dyspepsia, etc."

Other classifications were based on age, sex and occupation. The classification according to age divided the cases into three groups: children, adults and aged. A difference in the course of the disease is noted between children and old people. In the classification according to sex, emphasis is laid on the disastrous effects of parturition.

A classification based on occupation referred especially to the relation of dust to infection in the following trades: grinder, weaver, stonecutter, etc.

The first rational classification of the ancients was (1) phthisis incipiens, (2) phthisis confirmata and (3) phthisis desperata.

It is obvious that the necessity for classifying the various stages of chronic phthisis was recognized by the medical profession at a very remote period, long previous to the application of auscultation and percussion, as an aid in the diagnosis. Even at this early date the transitory nature of some chronic pulmonary affections was realized.

Bayle, who was not conversant with physical examination, from a pure anatomical study, added to the above three groups, (phthisis incipiens, phthisis confirmata and phthisis desperata), a fourth, which he believed preceded a demonstrable clinical beginning. He named this group *Phthisis occulta* or *Germe de la phthisie* and believed that the tubercle at this time was not developed sufficiently to produce symptoms. Bayle's first stage probably represents the incipient stage of the more modern classification.

Laennec, a pupil of Bayle, who, on account of his wonderful knowledge of physical signs was undoubtedly the best qualified clinician of his age to interpret correctly the needs of a classification for chronic pulmonary phthisis, divided it into three stages. His classification was based purely on anatomical grounds and the various stages were differentiated by means of physical signs. Symptoms were ignored entirely. The classification follows:

First stage. An accumulation of tubercles, detected by means of bronchophony and demonstrable dulness.

Second stage. Softening of the nodule, indicated by coarse râles, indefinite pectoriloquy and bronchial breathing.

Third stage. The discharge of the caseated material; that is, the stage of cavitation, with its accompanying physical signs.

Grancher (1890) preferred Bayle's classification and described in detail the clinical symptoms which gave rise to a suspicion of developing lung tuberculosis, previous to the appearance of dulness and râles as well as tubercle bacilli in the sputum. He describes it as the ***periode de la germination.***

A Fränkel (1902) criticizes Grancher's classification and believes that three stages are sufficient. He differentiates as follows:

First. Developmental period. General symptoms are manifest, while the local signs do not permit the absolute certainty of diagnosis.

Second. Pthisis confirmata. Pronounced infiltration and beginning ulceration.

Third. Progressive cavity formation.

Fränkel classifies certain special forms as follows:

1. Acute tuberculosis: associated probably with a latent focus: (a) circumscribed; (b) disseminated: pneumonic and broncho-pneumonic forms, the onset of which is frequently sudden: hemorrhage is mentioned as an early symptom.

2. Typically chronic tuberculosis: (a) pronounced fibrous; (b) bronchiectatic form; (c) Pleuritic form.

3. Tuberculosis of the young and aged.

Meissen felt that the extent of involvement had been over-emphasized in the above classifications and sufficient attention had not been paid to the virulence of the infection. The classifications indicated the degree of extension, but not the qualitative peculiarities of the disease which he felt were very important.

Brehmer (1860) the father of hygienic dietetic treatment, says very

little regarding the clinical forms of the disease and retained the classification introduced by the ancients: phthisis incipiens, phthisis confirmata and phthisis desperata. In a later publication, however, he recognizes a constitutional or hereditary and an acquired form. In his opinion, the first resulted usually from a disturbance of the circulatory apparatus, and he believed that the disease was caused by an abnormally small heart which failed to furnish sufficient nourishment to the lungs and other organs. The acquired form was due to a weakening of the constitution from various causes: dissipation, alcoholism, diabetes, parturition, etc.

Dettweiler, a pupil of Brehmer, emphasized the individualization of treatment and did not attempt division into groups.

A. von Sokolowski (1877), also a pupil of Brehmer, divides chronic tuberculosis into the constitutional and inflammatory types. These forms did not include miliary tuberculosis and phthisis florida. The constitutional form includes all hereditary phthisis and any phthisis caused by faulty nutrition, sexual debauchery, unhealthy living conditions, mental strain and the various dyscrasias. These occur mostly between the ages of eighteen and twenty-five and run, as a rule, an unfavorable course. The inflammatory or acquired tuberculosis begins with a "cold" or an acute inflammation of lung or pleura following measles, scarlet fever, etc. It also develops as the result of mechanical irritation from inhalation of irritating gases, etc. This occurs in all ages and attacks with preference the weak, although the robust are not immune. In this form the disease is generally limited to one lung and the course is, as a rule, slow and favorable. This classification is on the same plan as that of Brehmer, and in both cases the classifications were influenced by the teachings of Virchow, Niemeyer and others of the theory of the duality of tuberculosis. The above classifications are based on the assumption that the cases with a positive family history have an unfavorable course.

Meissen claims that he was the first to show that this was not the case, and that those with a positive family history had as good prospects of recovery as those with a negative family history.

Von Sokolowski (1891) made a further classification of the clinical forms, more especially the larval forms; that is, forms which mask themselves behind symptoms of other disorders. He included nine in this group; the pseudochlorotic, pseudocardial, pseudoscrofulous, pseudomalarial, pseudogastroïntestinal, pseudolaryngeal, pseudoëmphysema-

tous, pseudopleuritic and the pseudocroupous forms. This classification is interesting in that the protean onset of the disease is made clear.

The elder Loomis employed the following classification:

1. Caseous or catarrhal.
2. Fibrous.
3. Tuberculosis phthisis.

He emphasizes that the selection of climate must be governed by the type of case. The fibrous types do best in high altitudes. The caseous, especially if weak, do best in low altitudes with a moist atmosphere.

King's classification, which was first used at the Loomis Sanatorium in 1903, follows:

First. Early with mild symptoms. Patients with unmistakable evidence of pulmonary disease, demonstrable by physical signs, by the presence of tubercle bacilli in the sputum, or by the tuberculin test, but with very slight constitutional symptoms, such as fever, increased pulse rate, emaciation, etc.

Second. Early with severe symptoms. Constitutional symptoms severe, although the physical signs in chest may be almost imperceptible.

Third. Advanced with favorable symptoms. A more extensive local lesion than would permit of admission under the former division, while constitutional symptoms are very mild.

Fourth. Advanced with unfavorable symptoms. Same as preceding class, except that symptoms are unfavorable.

Fifth. Long standing with ulceration predominating.

Sixth. Long standing with fibrosis predominating.

Long-standing cases are described as those in which definite signs of the disease have been present for more than a year. King calls it, "an arbitrary classification, but yet one which is justifiable." He deems it unnecessary to explain further the subdivisions of the class, more than to say that the term "long-standing with fibrosis predominating" conveys the idea which in former years was understood by the terms "chronic interstitial penumonia," "old fashioned consumption," "chronic phthisis," etc. Although the addition of the long-standing classes makes this classification somewhat confusing to those who have not made practical use of it, I feel that King's idea is a good one, as it attempts to differentiate between those cases presenting lesions of the same stage, but with widely varying symptomatic pictures.

Beneke recognized three forms of phthisis. He claimed that the

patient's constitution and the etiology of the disease had not been sufficiently considered heretofore and felt that they are decisive factors in the prognosis and diagnosis of pulmonary tuberculosis. The classification of Beneke is as follows:

1. Fibrous.
2. Caseous: (a) catarrhal; (b) chronic pneumonic; (c) scrofulous.
3. Tuberculosis phthisis. This type is characterized by the development of miliary tubercles in the interstitial tissues, on the walls of vessels and in the bronchial submucosa. It occurs frequently in patients presenting marked habitus phthisicus, and the onset is characterized by sudden haemorrhage with expectoration of pure blood.

The fibrous form is generally observed in well nourished individuals with powerful frames and good musculature, who are capable of extended exercise. These cases may have repeated haemorrhages and present fibrosis of one or both apices; moderately fast pulse, but with good ventricular contraction; and a family history showing no scrofulous or phthisical tendencies, but which on the contrary, may show Bright's disease, gout, hepatic disease and cancer. In this form of phthisis there is hypertrophy of the interstitial tissue of the lung with or without bronchial catarrh and the process gradually leads to bronchiectatic cavities.

Caseous phthisis occurs in adolescence. The patients are under weight, slight of frame with rapid heart action, weak pulse, etc. Cavity formation may or may not occur. This class is sub-divided into:

a. Catarrhal form in which catarrhal symptoms predominate.

b. Chronic pneumonic form. Patients in this class have very little sputum, purulent in character. Nervous manifestations predominate.

c. Scrofulous form. This is characterized by indisputable signs of an earlier or present scrofulous disease.

Williams of the Brompton Hospital devised the following classification:

1. Acute tuberculosis: the miliary type.
2. Acute phthisis: the caseous pneumonia: phthisis florida type.
3. Scrofulous: accompanied by tuberculosis of the joints, glands, etc.
4. Catarrhal: with dominant catarrhal symptoms.
5. Fibrous: with predominance of fibrous tissue.
6. The usual chronic lung tuberculosis.

Cornet (1899) divided phthisis into two groups, the acute and chronic. There are, of course, cases which cannot be included in these two groups. There is, however, generally a transition of the disease from acute to

chronic and vice versa. This classification depends largely on the nature and onset of the disease, not on an anatomical basis. He emphasized that the onset of the disease may manifest itself as an anaemia, dyspepsia or an ill defined fever: "masked or larval forms," and called attention to the favorable termination of fibroid phthisis. Cornet also recommended the following schema, but felt that any classification was difficult to follow:

1. Incipient phthisis.
2. Stage of softening.
3. Stage of cavity formation.

L. Bard, who made a most complete study of classification, felt that the division of clinical groups, to be of practical use, should be reducible to an anatomical-pathological basis. The basis for this classification is explained in detail and cleverly presented. His classification follows:

1. Parenchymatous.
2. Interstitial.
3. Miliary.
4. Bronchitic.
5. Post-pleural.

The parenchymatous class is subdivided into:

a. Abortive.

b. Progressive: (1) caseous; (2) caseo-fibrous; (3) fibrous.

It may seem curious that Bard includes the fibrous form among the progressive forms; but those who have had extensive experience in tuberculosis recognize that this is as a rule progressive, although usually slow and relatively benign. Bard also describes in detail the fibrous form (chronic lung induration) with its action on the heart and the associated compensatory emphysema of the surrounding lung or in the opposite lung.

The caseous lung tuberculosis comprises acute, subacute and more chronic forms which may be transformed into the caseo-fibrous form. The caseo-fibrous form employed by Bard corresponds to our common chronic lung tuberculosis.

Interstitial class. In this class perilobular and periälveolar layers of connective tissue are more or less uniformly distributed between these structures.

The miliary, bronchitic, and post-pleural forms need no further explanation.

The following is the classification employed by the Hanseatic Assurance Institutions:

1. Simple catarrhal disease of one apex.
2. Simple catarrhal disease of both apices.
3. Widespread catarrhal disease.
4. Infiltration of a small extent of one apex, etc.

Turban criticizes this classification and argues that "the number of groups is too great and the definitions are too vague for a sharp separation of the groups." He is opposed to the term, "apical catarrh," which was widely used in Europe at one time, as it does not always indicate a tuberculous condition. A former patient of our institution was diagnosed as a case of right ' apical catarrh" by a Vienna clinician and upon admission to the Sanatorium shortly after coming to this country had definite right upper lobe tuberculosis with positive sputum. This patient had been told that she did not have tuberculosis.

Koeniger grouped his cases under the headings:

1. Slight.
2. Medium severity.
3. Severe.

In the "slight" form one apex was affected; in "medium severity" one or both apices affected to a greater extent than in the "slight" form; and in the "severe" form there was involvement of one or more whole lobes. Turban's criticism of this classification was that no regard was paid to the intensity of the process.

Turban's classification is based wholly on physical findings. He admitted at a later date, however, the necessity of including symptoms.

As taken from Brown's article on classification, Turban's scheme is as follows:

> Stage I includes those patients whose slight lesion does not exceed one lobe or two half lobes. Stage II includes those whose slight lesion extends further than Stage I, but at most to two lobes or a severe lesion extending at most to the volume of one lobe. Under Stage III are all not under I and II. "Slight lesion" is synonymous with infiltration and "severe lesion" with consolidation and excavation. Purely pleuritic dullness of slight extent is left out of account. Slight alterations in the breath sounds; for example, harsh breathing or prolonged expiration without change in percussion and without râles, are not to be considered.

Meissen modified Turban's classification by inserting a prophylactic state before Stage I, and a hectic stage after Stage III. Turban felt

that there was nothing to commend these stages and argued that the "prophylactics" are either healthy and altogether out of place in the schema or else fall into Stage I. and "the hectics may easily be distinguished in Stage III." He accepted as valuable, however, Meissen's suggestions to make two subheadings "according as fever is present or not," and further suggested that "F" should stand for high and "f" for moderate fever, the daily maximum limit for moderate fever to be 101.3°, as suggested by Strümpell. Turban proposed that the presence of mixed infection complications and the presence or absence of tubercle bacilli be denoted by signs and letters.

The German Imperial Board of Health used a modified Turban classification in their report on all patients treated in German institutions. The schema follows:

The side or sides affected is first indicated.

I. Slight, limited to a small area of one lobe, especially at the apex, and not extending below the clavicle nor the spine of the scapula, with or without fine, but without tympanitic râles.

II. Areas of the disease of wider extent than I, or less than III.

III. Involvement of at least a whole lobe or of several whole lobes, or signs of cavity formation.

The Turban-Gerhardt classification was adopted at the Vienna International Conference on Tuberculosis. This conference also advocated that the designation of the various stages should be supplemented by indicating the presence or absence of fever and of bacilli in the sputum. However, it appears that no great importance was attached to this addition to the classification at that time.

The Turban-Gerhardt classification follows:

I. Disease of slight severity, limited to small areas of one lobe; which, for instance, in case of affection of both apices, may extend beyond the spines of the scapulae and the clavicles: in case of affection of one apex, frontal, beyond the second rib.

II. Disease of slight severity, more extensive than I, but affecting at most the volume of one lobe; or severe disease, extending at most to the volume of one-half lobe.

III. All cases extending beyond II, and all such with considerable cavities.

By disease of slight severity is to be understood disseminated foci manifested by slight dulness, impure, rough or weak vesicular, vesiculobronchial, or bronchovesicular breathing and fine and medium râles.

By severe disease: compact infiltration recognized by great dulness,

very weak (indeterminate) bronchovesicular breathing with or without râles.

Considerable cavities, recognized by a tympanitic note, amphoric breathing, and extensive, coarse, consonating râles, come under Stage III.

Pleuritic dulness, if only of a few centimeters extent, is to be left out of account. If it is considerable, pleuritis should be specially mentioned under tuberculous complications.

The stage of disease is to be indicated for each side separately. The case, as a whole, is to be classified according to the more diseased side; for example, R II, L I–Stage II.

Brown criticizes this classification as follows:

> The objection to this classification is the unevenness of the distribution; and, while it divides the first group of Turban, which really needs division, the enlargement of the third group makes the Turban-Gerhardt classification of less value.

Trudeau's classification (1887) takes into account both the physical signs and local or general involvement.

I. Incipient. Cases in which both the physical and rational signs point to but slight local and constitutional involvement.

II. Advanced. Cases in which the localized disease process is either extensive or in an advanced stage, or in which, with a comparatively slight amount of pulmonary involvement, the rational signs point to grave constitutional impairment or to some complication.

III. Far Advanced. Cases in which both the rational and physical signs warrant the term.

Rufenacht-Walters supplements the Turban classification by noting the maximum temperature, pulse and loss of weight.

Schroeder and his co-workers while accepting the Turban classification, also note the nature of the pathological processes as caseous, caseo-fibrosis, fibrosis. The importance of dividing cases of chronic lung tuberculosis according to the extension of disease is generally recognized. The characterization of the clinical characters of the disease is considered, however, of still greater moment. It is felt that X-Ray examinations have clearly demonstrated that the disease is, as a rule, more extensive than is indicated by physical signs.

F. Penzoldt, (1909), assuming as established that all adults have tuberculous nodes, or remnants of such in the lungs, and that the majority do not suffer from clinical tuberculosis, classifies cases into latent and active. He prefers the German term "*stillstehende*" (quies-

cent) to the term "latent," since the term "quiescent" may include cases with definite physical signs.

A. Woodcock (1910) describes two types, those with resistance and those without resistance. The resistant ones have good weight, ample chest circumference in proportion to body height, rather broad than narrow hands, often enlarged neck glands, enlarged tonsils, broad nose, slow pulse and very slight tendency to fever. Acne of the skin is considered a good sign. Those without resistance show opposite characteristics.

Petruschky, von Pirquet, Hamburger and others differentiate the stages of tuberculosis according to the anatomical development of the tuberculous process: First. Primary with invasion of the lymph glands by the bacillus. Second. Secondary with gradual development of the tubercles in the tissues, bones, joints, skin, lungs, etc. Third. Tertiary with destruction of tissue and entrance of mixed infection. In regard to the lungs, although this stage indicates chronic lung tuberculosis, it may also include some acute cases. This classification corresponds to the one employed for syphilis. The first two stages are called closed tuberculosis; the third, open tuberculosis. The first two divisions come under the head of early tuberculosis; the third as a later stage of this disease. The first two stages call forth at times doubtful symptoms, constitutional weakness, anaemia, etc. Enlarged mediastinal glands and other glands in the apex of the lung are often demonstrated at autopsy and may give rise to symptoms. These foci often remain harmless, may become obliterated (abortive) or under peculiar conditions become active and produce clinical manifestations. Petruschky's classification is most interesting but of no great value, as it is not specific enough to cover the various types of pulmonary cases met with in sanatorium work.

H. Schut attempts a classification based on the history, the results of physical and X-ray examinations, and the pathological anatomy. He also emphasizes that any classification, to be of great value, must be indicative of the prognosis of the disease. Schut feels that Turban's classification covers the average run of cases satisfactorily. In his opinion, however, it should be supplemented by the clinical character of the case; that is, by the designations caseous, fibrous, and in doubtful cases, caseo-fibrous, also by remarks concerning the presence or absence of fever, positive or negative sputum. He feels that only by this method can one classify the clinical groups so that they are available for accurate statistical data. Schut's classification follows:

I. Obsolete tuberculosis. Schut considers this form only of scientific interest.

II. Clinical tuberculosis. Clinical tuberculosis is divided into latent and manifest.

a. Latent. The clinical findings suggest the presence of a tuberculous node somewhere in the body which cannot be localized. Symptoms may or may not be present, depending on the susceptibility of the individual affected.

b. Manifest. The symptoms are definite.

The manifest form is subdivided into two principal forms: 1. Proliferative; 2. Exudative. The manifest form, if early treatment is instituted, may be converted into the latent form. The latent and manifest forms are described by Schut in great detail. According to Schut there can be no sharp division between the chronic and acute forms. There exist many transition forms with subacute or even more slowly progressive forms, depending on the extension of the disease and its intensity. In the differentiation between acute and chronic disease. the presence or absence of fever is of decided importance. General chronic lung tuberculosis is distinguished by a mixed form consisting of caseation and destruction of tissue (exudative), and fibrosis with scar formation (proliferative). These conditions are present in varying degrees. There is, especially at the beginning of the disease, a tendency towards fever though this may be entirely absent. The behavior of the heart, even in the absence of fever, is of some value in distinguishing the two types. Rapid pulse is an unfavorable indication and vice versa. The caseous form is most often observed in those with a deficient body structure and chest development and of asthmatic constitution, while those with a powerful physique, "not necessarily always associated with a good body weight and rosy complexion" are most liable to suffer a fibroid form of disease.

Individuals with a proper ratio between height and chest measurement show the fibrous form more often than those with a thorax approximating the habitus phthisicus.

Schut also points out that those who are tall and thin are often tough, and possess a good constitution, and that corpulent, flabby individuals often do not show a good resistance. Patients in middle age incline to the fibrous, the adolescents to the caseous form: the exceptions are generally due to diabetes, alcoholism, etc. Fibrous types are predisposed to haemorrhages which may be copious. Fever, however, is infrequent. Acute exacerbations with extension of the disease are also

infrequent, and the sputum contains fewer and less virulent organisms. Complications of the larynx run a more benign course with a tendency to become quiescent, with the development of scar formation.

The American Climatological Association's Classification, which follows, is based principally on Trudeau's schema.

Incipient. Slight physical and subjective signs, with history indicative of pulmonary tuberculosis. Sputum, if present, is without bacilli.

First stage. Definite physical signs of localized infiltration; total involvement of less than half a lobe, whether at one or more points; cough and expectoration with bacilli; constitutional symptoms slight. (In disseminated cases, expectoration and bacilli may be absent with constitutional symptoms more severe).

Second stage. Infiltration of single or multiple areas approaching or equal in amount to one lobe; or small area in stage of softening; cough and expectoration with bacilli; constitutional symptoms severe.

Third stage. Infiltration in excess of one lobe or, if less, in stage of well-developed excavation; more severe constitutional symptoms.

We now come to the classification of pulmonary tuberculosis adopted by The National Association for the Study and Prevention of Tuberculosis, which is in general use in this country:

The following definitions indicate the furthest extent of disease and the greatest severity of symptoms that a patient can present and still belong to the stage defined. All patients beyond the Incipient stage fall under the Moderately Advanced stage, unless the physical signs and the symptoms exceed those of the Moderately Advanced stage, when they should be classified as Far Advanced.

Incipient

Slight or no constitutional symptoms (including particularly gastric or intestinal disturbance or rapid loss of weight), slight or no elevation of temperature or acceleration of pulse at any time during the twenty-four hours. Expectoration usually small in amount or absent. Tubercle bacilli may be present or absent.

Slight infiltration limited to the apex of one or both lungs or a small part of one lobe. No tuberculous complications.

Moderately advanced

No marked impairment of function either local or constitutional.

Marked infiltration more extensive than under incipient, with little or no evidence of cavity formation. No serious tuberculous complications.

Far advanced

Marked impairment of function, local and constitutional.

Extensive localized infiltration or consolidation in one or more lobes. Or disseminated areas of cavity formation. Or serious tuberculous complications.

Acute miliary tuberculosis

The above classification is an improvement over the classifications which preceded it. Each of the three stages, Incipient, Moderately Advanced and Far Advanced, is based on certain specified pathological findings and clinical symptoms. The lesions and symptoms, however, are not interchangeable, but are immobilized in each of the three stages. This has been a source of confusion, especially to men in sanatorium work, as many cases with moderately advanced and some with far advanced lesions, present nothing beyond incipient symptoms, while others with incipient lesions present moderately advanced symptoms, etc. If the lesions and symptoms of the various stages are listed under separate headings, then the above discrepancies are obviated, and it is possible to classify any given case in accordance with the extent of pulmonary involvement and nature of the symptoms.

The following rearrangement of the National Association Classification was worked out at Otisville in 1910 and adopted by the American Sanatoria Association at the Mid-Winter Meeting, December 7, 1916:

These combinations are interpreted as follows:

Lesions

Incipient. Slight infiltration limited to the apex of one or both lungs, or a small part of one lobe. No tuberculous complications.

Moderately Advanced. Marked infiltration, more extensive than under incipient, with little or no evidence of cavity formation. No serious tuberculous complications.

Far Advanced. Extensive localized infiltration or consolidation in one or more lobes. Or disseminated areas of cavity formation. Or serious tuberculous complications.

Symptoms

A. (*Slight or None*). Slight or no constitutional symptoms, including particularly gastric or intestinal disturbance, or rapid loss of weight; slight or no elevation of temperature or acceleration of pulse at any time during the twenty-four hours. Expectoration usually small in amount or absent. Tubercle bacilli may be present or absent.

B. (*Moderate*). No marked impairment of function, either local or constitutional.

C. (*Severe*). Marked impairment of function, local and constitutional.

Acute Generalized Miliary Tuberculosis.

This schema offers the following combinations:

Incipient A.	Moderately Advanced A.	Far Advanced A.
Incipient B.	Moderately Advanced B.	Far Advanced B.
Incipient C.	Moderately Advanced C.	Far Advanced C.

Incipient A. An incipient lesion with symptoms of the present incipient stage. Incipient B. An incipient lesion with symptoms of the present moderately advanced stage. Incipient C. An incipient lesion with symptoms of the present Far Advanced Stage. Moderately Advanced A. A moderately advanced lesion with symptoms of the present Incipient stage. Moderately Advanced B. A moderately advanced lesion with symptoms of the present Moderately Advanced stage. Moderately Advanced C. A moderately advanced lesion with symptoms of the present Far Advanced stage. Far Advanced A. A far advanced lesion with incipient symptoms, etc. The rearrangement unquestionably greatly increases the flexibility of the classification without appreciably modifying the original text.

CHRONIC NON-TUBERCULOUS LUNG INFECTION[1]

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The material for this study consisted of nine cases of chronic non-tuberculous lung infection of long standing—four years or more—and is of interest inasmuch as careful history and physical examination had previously determined the diagnosis as tuberculosis. The disproof of the diagnosis of tuberculosis was justified after long study, comprising a review of the factors in the history, frequent physical examination, X-ray photography of the chest, and repeated bacteriological study of the sputum. The term "chronic non-tuberculous lung infection"[2] may be too inclusive but it seems to be the best generic name for the particular type of case here presented.

These cases were diagnosed as supposed cases of tuberculosis by the most experienced physicians sending patients to Ray Brook for the treatment of tuberculosis and are therefore not the result of careless or inexperienced examination. The mistake in diagnosis is of interest as leading to the discovery of some procedure that will avoid this error, thereby saving time and removing the handicap incurred in condemning the patient because of the apparent extent of a lesion seemingly tuberculous.

The existence of chronic secondary infections of long standing in organs other than the lungs has been sufficiently pointed out: chronic cardiac valve infections, chronic joint infections and chronic infections of abdominal viscera have been carefully and fully described. The specific etiology and course of infections in these locations are better described than those of similar infections occurring in the lungs.

Chronic non-tuberculous lung infections may be caused by a variety of organisms. This study seems to point to the influenza bacillus as the most frequent predominating sputum organism and as the most probable etiological factor. The pneumococcus and streptococcus have also been found as predominating organisms, and an undetermined Gram negative bacillus was isolated in one case of ten years clinical duration.

[1] Clinical section by Dr. Garvin. Laboratory section by Dr. Lyall and M. Morita.

[2] Hamman's designation.

CLINICAL COURSE

The origin of the lung disease may date subsequent to some remote acute infection, such as measles or whooping cough. It may also come on insidiously as an indefinite cold on the chest beginning either in the summer or in the winter.

The clinical course following the initial infection is that of slight cough and expectoration which may be continuous throughout the year or in the first few years of the disease may manifest seasonal variations, being worse in the winter months and almost or completely disappearing in the summer months. The reverse of this may also occur, the cough and sputum being worse in the summer than in the winter.

In course of time the general health becomes affected. The patient notices that the endurance is waning and cough and expectoration becoming more than an inconvenience. The symptom complex is complicated with more numerous acute exacerbations of "grippe." Medical observation at first is necessitated for these acute exacerbations. At this stage the patient may present no suspicious inspection, auscultatory or other signs suggestive of pulmonary tuberculosis. The general outward appearance continues good. Ultimately, under unfavorable environment, the general health fails, cough and expectoration increase, other complications occur, and the patient is suspected as tuberculous, and such a diagnosis is made as the most probable one in the absence of other understood infection and for the reason that tuberculosis is the most probable chronic lung infection.

The ease of error and the difficulty in diagnosis from history and examination are not apparent from this brief description because the clinical course of the disease is not at first clearly described by the patient. The break-down in health is usually ascribed by the patient to some recent episode that suggests pulmonary tuberculosis to the examiner: rapid loss of weight, loss of appetite, the sudden onset of cough and expectoration, and possibly the occurrence of a pulmonary haemorrhage. It is only after repeated reviews of the history coincident with repeated examinations that the true sequence of events becomes clear in the patient's mind and only then is it possible for the examiner to arrive at a fairly accurate account of the clinical course of the disease.

All the symptoms which occur in pulmonary tuberculosis may occur

in chronic non-tuberculous lung infection. This is the principal reason for error in diagnosis. The major symptoms are periodic cough and expectoration, beginning insidiously, disappearing, reappearing, and finally becoming chronic with purulent sputum, the daily amount of which varies from 5 to 60 cc. At times expectoration may be so slight that it amounts to only from 1 to 3 cc. every second or third day. There are periodic attacks simulating grippe, frequent colds, occasional attacks of slight fever, and sweats that are described as cold at night. Not infrequently, pulmonary haemorrhages occur during a state of rapidly waning health, so that the diagnosis of pulmonary tuberculosis is suggested from symptoms alone. Tubercle bacilli, however, are never found.

PHYSICAL EXAMINATION

Physical signs in the ordinary sitting or standing position may or may not differ from those of pulmonary tuberculous infiltration. Inspection usually shows a normal chest appearance with fair nutrition. Palpation may reveal a ronchus. Auscultation with or without the aid of cough may reveal few or numerous râles without suggestive breath sound change. The râle area is predominantly located below the middle of the chest; so predominantly that râles of long standing below the middle of the chest (in the absence of a heart lesion) are almost as diagnostic of chronic non-tuberculous lung infection as râles of long standing at the apices or upper half of the chest are suggestive of pulmonary tuberculosis.

Pulmonary tuberculosis is frequently a disease with a wealth of physical signs and a poverty of symptoms. This is so marked that often it seems strange that with the presence of so much disturbance in the chest, the patient is so little inconvenienced.

DIAGNOSIS

In chronic non-tuberculous lung infection, the reverse is true. One strives to make the physical examination parallel the symptoms that are present. Patients may expectorate enough sputum to justify the suspicion of bronchiectasis without the hearing of a single abnormal physical sign or a single râle in the chest. If no signs are heard in the sitting or standing position *examination in the inverted position* while lung drainage is in progress will often reveal the site of the infected area

when it could not be discovered otherwise. The point of disparity of physical signs and symptoms to that of pulmonary tuberculosis is thus made. Upper lobe non-tuberculous infections present more difficulty in differential diagnosis. In this type of case a long period of observation, the constant presence of another microörganism in the sputum, the continuous absence of the tubercle bacillus and the absence of X-ray findings suggestive of tuberculosis may determine the diagnosis as chronic non-tuberculous lung infection.

The differential diagnosis is concerned with five principal points: (1) duration of disease, (2) state of general health, (3) location of lesion, (4) number of physical signs and (5) number of symptoms, particularly cough and expectoration.

The principal differential diagnosis to be made is that from pulmonary tuberculosis. There will usually be observed a very striking disparity of these points in favor of chronic non-tuberculous lung disease and against tuberculosis except at such times when acute exacerbations occur, when the differential diagnosis will not be possible and the diagnosis will be that of tuberculosis because symptoms or signs, or both, strongly suggest it. Usually the duration of the disease is clinically longer with less severity of effect upon the patient than would be expected if the disease were tuberculosis.

Base lesions in tuberculosis are usually quite toxic and progressive. Base lesions of chronic non-tuberculous type are rather non-toxic and non-progressive. The general health appears to be very much more satisfactory than would be expected if the patient were tuberculous.

As regards location, ninety per cent of all tuberculous lesions are located in the apices or upper lobes of the chest, and but ten per cent in the lower lobes. In chronic non-tuberculous lung infection, the reverse of this is true.

The physical signs will be at considerable variance to what might be expected if the condition were tuberculous. Two extremes may be met. There are either a large number of rather moist râles and ronchi with only moderate cough and expectoration, or very few or no physical signs in the presence of symptoms. The symptoms, particularly cough and expectoration, are usually more manifest than the signs.

The differential diagnosis of bronchiectasis of extensive degree is not difficult. The effect of posture may be used to observe any increase in signs and the development of unsuspected râle areas. Determinative bacteriological study will then place the diagnosis as accurately as it may at present be done.

TREATMENT

The essential treatment is posture. As the lesion is usually at the base of the lung, drainage by the inverted position is necessary in order to remove the muco-purulent sputum which is not easily accomplished in the erect position and also to relieve pressure and absorption symptoms that are due to retention of the secretion. Examination in various inverted positions will often determine the best posture for drainage. The experience of the patient may also be used to determine this. The patient is instructed to assume this posture and is advised to vary it as the result in lung drainage is indicated. Posture is of striking therapeutic benefit even in cases with very slight sputum retentions of 1 to 2 cc. Some illustrations are introduced to exhibit postures which are effective: the Trendelenberg, the reversed Trendelenberg (face down), directly on head over the foot of the bed, the use of a chair head down, etc. For convenience in posture, the purchase of a cheap Buchanan table is advisable for those who can afford it.

Lung drainage should be continued for a period sufficient to cleanse the respiratory tract thoroughly. At least fifteen minutes four times a day is a minimum rule. The hours most convenient and most productive in performing the lung toilet should be selected.

The initial treatment may cause a brisk reaction with fever, but this promptly subsides. With continued treatment, there is a rapid improvement of general condition and the sputum is gradually diminished to complete disappearance or to a minimum residuum that persists. Chronic nasal sinus infections are a frequent complication and usually require attention before postural treatment can be successfully carried out. When the maximum therapeutic result is obtained the patient is prone to become careless and neglectful of postural drainage. If a residual sputum continues when the maximum therapeutic point has been reached, drainage must be continued regularly and must be added to the daily toilet procedures. It may be advisable to place the patient in the country for six months to a year. The substandard physical condition and the long standing infection makes the out-of-door rest regimen advantageous.

PLATE 1

FIG. 1. POSTURE: THE USE OF THE FOOT OF THE BED
FIG 2. POSTURE: INVERTED POSITION, USE OF CHAIR
This is the most practical and useful position for routine treatment

FIG. 2

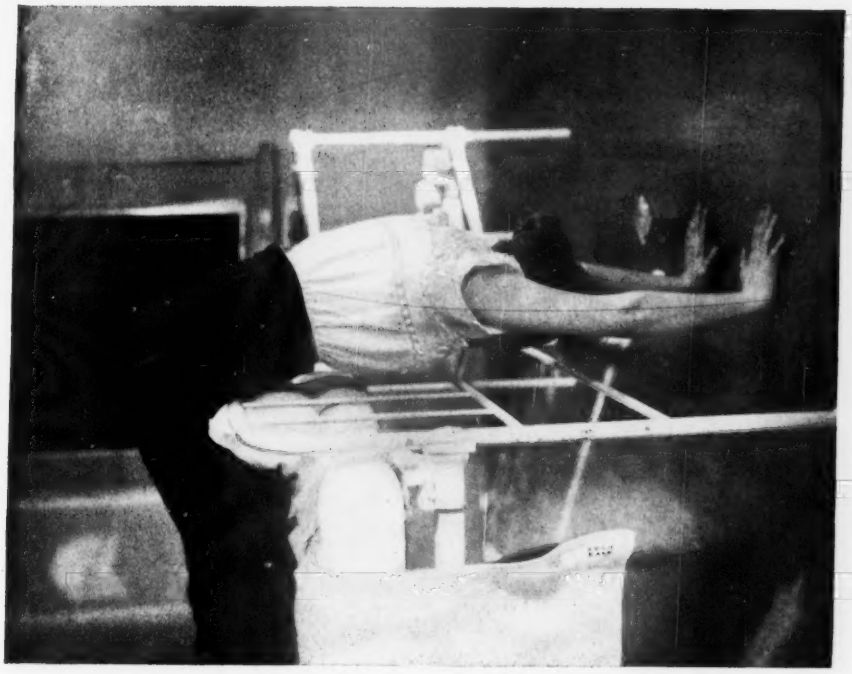

FIG. 1

PLATE 2

FIG. 3. POSTURE: PRONE TRENDELENBERG POSITION, USE OF TABLE
FIG. 4. POSTURE: TRENDELENBERG POSITION, USE OF TABLE

FIG. 3

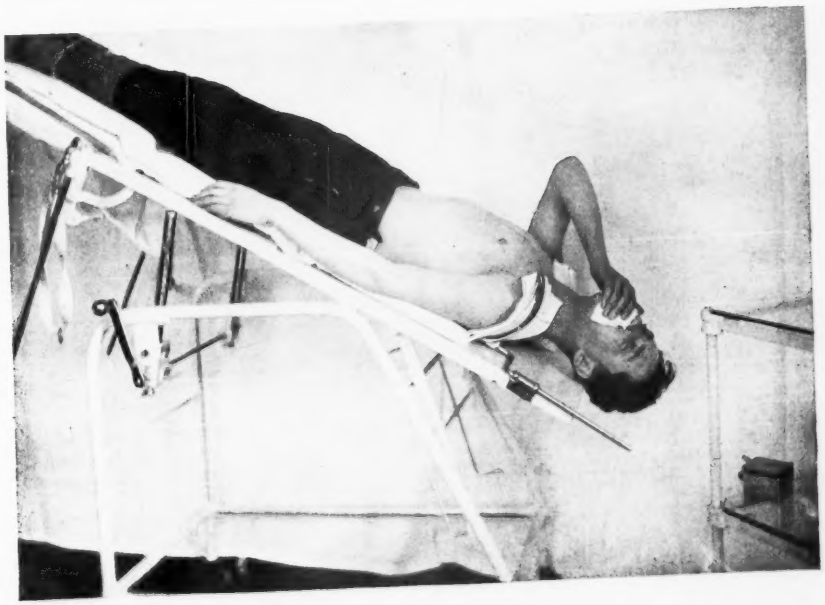

FIG. 4

PLATE 3

FIG. 5. THE FOURTEEN-HOUR RETENTION OF A CASE OF CHRONIC NON-TUBERCULOUS INFECTION

Total sputum shown. Note the numerous *very small* ball like masses which consist of almost pure culture of bacillus influenzae. The case is of ten months' duration. Sputum obtained by fifteen minutes' posture.

FIG. 5

PROGNOSIS

The prognosis in younger patients is excellent. Proper pulmonary toilet and a period of country rest may place them for the first time among the effective workers. They should be limited to clean and non-dusty employments on account of their proneness to repeated attacks of acute respiratory infections, but if diligent about lung drainage they need not be limited in the ordinary ambitions of life, certainly not to the extent that the tuberculous individual with the same extent of lesion is limited.

The relation of the bacterial carriers of the chronic non-tuberculous lung type to healthy and other associates is discussed in the bacteriological section of this paper.

A few case histories are abstracted. In all cases here reported the Wassermann reaction was negative and tubercle bacilli were never found after repeated search.

CASE HISTORIES

Case 2660. Female, age 23 years, American, single, clerk.

Family history and personal history unimportant. Patient noticed that she was sustandard for four years previous to onset of disease. No symptom during this period except weakness, and no definite medical diagnosis made. The physical substandard state was perhaps correctly ascribed to family and financial worry, terminating in the death of the mother from cardio-nephritic disease. The patient weighed 97 to 105 pounds (normal weight 124). During this period she was treated with tonics and over-feeding without effect. During this period too her lungs were normal, although suspected. July 4, 1912, suffered from a severe attack of "grippe," lasting about a week, temperature 104°; was needled for fluid at right base posteriorly, but none obtained. After recovery, she left for a period of country rest and improved. Now for the first time, she became aware of a very little cough and expectoration. Râles were discovered at right base posteriorly. Diagnosis of tuberculosis made, treatment postponed, diagnosis remade and the patient was finally sent to Ray Brook.

On entrance, February 14, 1913, the patient was inverted to drain suspected right base posterior lesion, because of posterior base râles, but no sputum was obtained (the wrong posture was used as was subsequently discovered). The patient gained nine pounds. Posterior râles disappeared, and then it was discovered that the true Trendelenberg was the correct position for draining this patient. The location of the infection was principally in the

right lower lobe anteriorly which gave no physical signs before, but numerous râles after drainage. The amount of sputum by correct lung toilet was 2 cc. consisting of very small millet to small pea like balls, ten to twenty in number, which consisted of almost a pure culture of the influenza bacillus. Physical signs before drainage were frequently absent. After drainage numerous râles occurred, much increased with the aid of cough. The patient gained seven pounds additional weight and returned to work after a treatment period of eight months and has been in apparently normal health since (three years).

Case 3385. Male, age 45 years at onset, 49 at death, Scotch, married, clothing salesman.

Past history unimportant. No previous illness for seventeen years. In summer of 1912, developed a "cold on the chest" which caused a cough with very slight expectoration and was treated for bronchitis. Health gradually waned, lost eighteen pounds, and by January 1, 1913, (about five months after onset), was compelled to cease work on account of weakness, cough and slight expectoration. Went to the country. This physical substandard state continued and he was admitted to Ray Brook, October 1, 1914, two years after the onset of the disease.

Physical examination on entrance revealed an emphysematous chest with resonant râles throughout, rather asthmatic type. X-ray showed increased general lung fibrosis. Sputum which was very small in amount (5 to 10 cc. daily) contained almost a pure culture of the influenza bacillus which was continuously present during the entire observation period of the next two years. Postural treatment was attempted without effect, owing to the general distribution of the infection in the bronchial tree. This physical state continued for two years, patient becoming progressively weaker with general exhaustion accompanied by myocardial failure. Moderate general anasarca caused death.

At autopsy the lungs showing a general increased fibrosis as the major finding. There was slight and obsolete tuberculosis of the bronchial glands and of the left apex.

Case 3384. Male, age 34 years, single, salesman.

Early history unimportant. Went to school at seven and began work at thirteen. Onset at age of twenty-four. First conspicuous symptom came on while laughing when he had a sudden haemorrhage. After this he had cough and expectoration of about 20 cc. daily. Was ordered to the country for a few months, gained weight and lost cough partially. Subsequently this story of haemorrhage, cough and expectoration was repeated three times, and the patient was admitted three times to different sanatoria with diagnosis

of tuberculosis. Tubercle bacilli, however, had never been found in the course of ten years. In retrospect the patient thinks he had a slight cough and expectoration before his first haemorrhage.

Physical examination showed good general condition. The right apex gave râles after cough, of localized character, so typical that the patient was an "excellent demonstration case" for the physical signs in the usual incipient, apical, tuberculous lesion. Occasional scattered râles at other points. Posture (reversed Trendelenberg) gave 1 to 5 cc. of rather fluid, purulent sputum which always contained an unclassified Gram negative bacillus. X-ray showed at the right root a peculiar small triangular shadow constantly present; apices not definitely infiltrated. Patient drained by inversion four times a day. Sputum would often disappear for ten day periods.

This case so closely simulates tuberculosis that error is justifiable and the case is included as non-tuberculous because our observation of it has extended over the ten year period.

Case 3597. Female, age 21 years, single, American, librarian.

Patient states that she was delicate as a child. "She took cold easily." At thirteen an attack of right lung pneumonia and pleurisy occurred, lasting ten to fourteen days; patient not very ill. At high school the cough and expectoration increased greatly. In the summer and winter of 1912 it disappeared entirely. In spring of 1913, it again recurred and gradually increased. In autumn of 1913 had an attack of right base pleurisy diagnosed as tuberculous. Entered a sanatorium and lost cough and expectoration in winter of 1913. Returned home in spring, and in fall of 1914, cough and expectoration recurred. Same cycle repeated. Admitted to Ray Brook, May 8, 1915.

Physical examination revealed excellent general condition, slight cough and expectoration, râles at right base, increased after drainage in reversed Trendelenberg position. Sputum, 5 cc. daily; tubercle bacilli never found. The sputum contained an influenza bacillus in almost pure culture. Posture rapidly caused sputum to cease and patient regained excellent general condition with no symptoms and no signs.

There was a high blood pressure, 260 to 270 mm., with a faint trace of albumen and an occasional cast in the urine. Kidney elimination (sulphonephenolphthalein) was 25 per cent the first hour. Traces only after that. The kidney complication was not previously known to the patient who had been in competent medical hands and it was supposed to be a secondary development.

Case C. R. M. Physician, age 26 years at onset of disease, October, 1910. Present age 32 years.

Family history not important.

Personal history: A left middle ear discharge since childhood. Radical

mastoid operation in summer of 1909. No discharge from ear for three years. Epidermic accumulations have caused annoyance several times since. Had ordinary diseases of childhood and was not considered robust as a child. While attending preparatory school was very active, ran a two mile, one mile and quarter-mile race in one afternoon. Completed medical course with apparently normal health.

Present illness began October, 1910, with a severe cold. Cough persisted with slight expectoration; by Christmas noticed an occasional night sweat; lost weight and had sticking pains in chest. April, 1911, diagnosed as tuberculous, first at the apex then at the base; was treated in a sanatorium, gained twenty pounds and lost cough. In summer, 1911, had an acute attack of "grippe" with temperature of 102° for three or four days. Subsequently was again admitted to a sanatorium and had fever of 99° to 99.2° frequently in the evening, for the next two months. Cough and expectoration practically disappeared. In April, 1912 had another acute attack of grippe. Cough and expectoration returned but gradually disappeared in the summer. Had occasional attacks of left base pleurisy at this time. In winter, 1915, was unusually well and became very active physically. In February, 1916, had another attack of grippe which left a cough of slight hacking type. Did not recover, and decided his "tuberculosis" was again annoying him.

Subsequent course: Examination now suggested chronic non-tuberculous lung infection of right base posteriorly and slightly anteriorly. Patient was systematically drained. A small broncho-pneumonic patch to the right of the heart was discovered by X-ray. After six months, the area completely disappeared as also did the physical signs and symptoms. The influenza bacillus was so predominant in the sputum as to be present in almost pure culture. Tubercle bacilli were never found during a five year observation period.

Following systematic drainage in the Trendelenberg position, the sputum diminished from 5 cc. daily to from 1 to 3 cc. every second to third day, and after six months disappeared entirely. The small broncho-pneumonic patch slowly cleared up and the X-ray shadow disappeared.

BACTERIOLOGICAL STUDY OF THE SPUTUM FLORA IN CHRONIC NON-TUBERCULOUS LUNG INFECTIONS

TECHNIQUE

Collection of sputum. Since the focus is located in the lower parts of the lung and expectoration is difficult, the collection of a specimen may be attended with some difficulty. However, sputum can usually be obtained if the patient is inverted and a persistent attempt made. It may be necessary to invert the patient head down for as long as fifteen

minutes before a satisfactory base specimen is obtained. The residual or the deepest sputum specimen must be collected for examination. In two cases the influenza bacillus that was present in almost pure culture in such specimens could have been easily missed if great persistence had not been used in obtaining the very residual sputum. The sputum is collected in a sterile petri dish and immediately examined. The sputum thus obtained unquestionably comes from the seat of the lesion. The proof of the origin of the sputum was undertaken in a case not here included of a double base abscess of the lung. A small anterior communicating base abscess and a large posterior non-communicating abscess occurred in the same patient. The injection of methylene blue, 1 per cent solution, into the small anterior abscess, was expectorated before the needle could be withdrawn. Later a similar experiment was carried out on the posterior non-communicating abscess with the result that the methylene blue was eliminated by the kidney. It is inferred that the sputum obtained in the cases here reported undoubtedly came from the lesion.

Microscopic examination of the sputum was made at once. One specimen was stained by Gram's method which gave the number of organisms present and the probable number of blood agar plates necessary for isolation of types. The second specimen was stained by the Ziehl-Nielsen method for acid fast bacilli.

A small piece of sputum, about the size of a pea, was rubbed up in a sterile mortar with a little nutrient bouillon. Five-tenths to 1 cc. of this mixture was injected into the peritoneal cavity of a white mouse weighing 15 to 20 grams. Upon the death of the animal, if this occurred, an aseptic autopsy was performed and cultures were made from the peritoneal exudate and heart's blood upon plain agar, plain beef broth, and rabbit-blood agar with a reaction plus 0.3 to plus 0.6 to phenolphthalein. Smears were taken of the heart's blood and peritoneal exudate, and capsule and Gram stains were made.

A second specimen of sputum was washed through several changes of sterile saline according to the Kitasato method as modified by the Saranac Laboratory. Half of this specimen was dropped into a tube of ascitic broth for a mass culture. The second half was smeared over the surface of three or four rabbit-blood agar plates by the Conradi method. After such plating, isolations were made and each organism carefully studied.

In August, 1915, eight cases were examined. The following chart presents a summary of the findings obtained.

TABLE 1

CASE NO.	BACILLUS INFLUENZAE	STREPTOCOCCUS MUCOSUS	PNEUMOCOCCUS MUCOSUS	STREPTOCOCCUS HAEMOLYTICUS	STREPTOCOCCUS NON-HAEMOLYTICUS	GRAM NEGATIVE COCCUS	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS AUREUS	DIPHTHEROID	GRAM NEGATIVE BACILLI	PNEUMOCOCCUS
1	1	2	—	—	3	—	4	5	—	—	—
2	2	3	—	—	1	4	5	—	6	—	—
3	—	—	3	—	1/2	1/4	—	—	—	1	—
4	1	—	—	3	4	2	+	—	5	—	—
5	1	—	—	—	2	3	—	—	—	—	—
6	1	—	—	—	3	2	4	—	—	—	—
7	2	—	—	—	—	3	4	—	—	—	1
8	2	1	—	—	—	3	—	4	—	—	+

The numbers indicate the order of predominance. The predominating organism is usually present in great excess over all other organisms. The second, third, fourth, etc., order of predominance indicates from a moderate number to exceedingly few accompanying organisms. Where a fraction is used the upper number indicates the place in frequency of organism, and the lower number indicates the number of different strains observed.

BACTERIOLOGICAL FINDINGS

Cultural Identification. B. Influenzae. Small Gram negative bacillus* Some strains exhibit a slightly longer form and show more involution types than others. Some maintain a short typical coccoid form. No marked change beyond this was observed under artificial cultivation during the course of fifteen months, and in over a hundred and fifty generations. Culturally, the organism is strictly haemoglobinophilic, never growing on haemoglobin-free media, although growth occurs on agar containing blood in a high dilution. All the strains studied were killed by exposure to a temperature of 53°C. for ten minutes. Blood from the rabbit, sheep, guinea pig, man and horse, was used in varying dilutions up to 1 to 500. This was mixed with plain agar at 40°C., also at 90°C. for the purpose of comparison. There appeared to be no distinct optimum point of growth in the haemoglobin dilutions. All dilutions of haemoglobin or methaemoglobin gave good results. A dilu ion of 1 to 10 was used for routine cultures and 1 to 50 for vaccine growth. Rabbit, guinea pig and human blood gave the most favorable results, even at high dilutions.

The colonies were very small on dry or unfavorable blood agar, and

relatively large and luxuriant on moist and favorable blood media. They were transparent, and produced no haemolysis and no other change on ordinary blood agar except perhaps a diffuse darkening of the media.

Viability. The strains of B. Influenzae here isolated remained viable in the incubator at 37.5°C. for from nine to thirteen days, at room temperature for seven days, and in the ice box for five days. Occasionally strains died before the fifth day in the ice box. Growth from cultures kept at incubator temperature could not be depended upon after the ninth day.

Symbiosis. Colonies of the influenza bacillus were observed to grow much larger about colonies of certain other organisms. Attempts were made to grow the bacillus influenzae on haemoglobin-free media with living and dead cultures of the staphylococcus aureus, streptococcus mucosus, pneumomucosus, streptococcus haemolyticus, streptococcus non-haemolyticus, diphtheroids, various Gram negative cocci isolated from the sputum and with one unidentified Gram negative bacillus which appeared to favor particularly the growth of bacillus influenzae in its immediate environment on haemoglobin containing media.

The technique of this experiment was as follows:

1. With live organisms.

A non-haemoglobin-containing ascitic agar plate was streaked with a fine platinum needle with the organism to be tested in such a manner that the colonies of the resulting growth would be discrete. Over this at the same seeding, the bacillus influenzae was planted by smearing the surface with a platinum loop. The plates were incubated for five days and examined daily.

2. With dead organisms.

Twenty cubic centimeters of plain agar were placed in 6-ounce bottles and slanted, inoculated with the organisms to be tested, and after twenty-four to forty-eight hours incubation were autoclaved for fifteen minutes at fifteen pounds, shaken while hot and poured into a sterile Petri dish, cooled and inoculated with bacillus influenzae, incubated for five days and examined daily.

All such attempts with living and dead organisms were negative.

Pathogenicity for laboratory animals. White mice withstood 0.5 cc. of a turbid vaccine equal to one-tenth of a tube slant of a forty-eight hour culture. A whole tube slant of a four day culture killed mice from toxicity rather than pathogenicity in from fifteen minutes to six hours. Rabbits withstood apparently without effect one forty-eight

hour blood agar slant, as well as 4 square inches of forty-eight hour surface growth on rabbit blood agar. The entire growth from as high as seven forty-eight hour blood agar slants failed to kill guinea pigs when injected intraperitoneally.

Immunizing experiments. The organisms seemed to be toxic in large quantity, either in the living or killed state. As the doses were increased, in the course of immunization, many animals succumbed. At the end of three months immunization no agglutinins were demonstrable. Agglutination was attempted both macroscopically and microscopically with an emulsion of the organism in physiological salt solution incubated at 37° for varying lengths of time. The serum was used in dilutions of from 1 to 10 to 1 to 100.

Two series of rabbits were inoculated intravenously with increasing doses at five to seven day intervals, one series with killed cultures, the other with living organisms. Killed cultures were obtained by growing the organism on a large rabbit blood agar slant in a six ounce square wide mouthed bottle for from twenty-four to forty-eight hours, washing off with physiological salt solution and heating at 60°C. for thirty minutes. The square surface of this medium made it measurable and the dose was figured in growth from square inches. Living organisms were obtained by growing them in ordinary rabbit blood agar tubes and were suspended in physiological salt solution. The growth from one agar slant was given as the initial dose and this was subsequently increased by one agar slant at each dose up to four slants. At this point, 50 per cent of the animals died. After the fourth injection, the surviving animals were bled every ten to fifteen days and agglutination attempted with the homologous strain as antigen. Twenty-eight animals were used.

The differentiation of streptococci and pneumococci is based on the haemolytic property in vitro, the bile solubility and the ability to ferment various carbohydrates. In the differentiation of this group, the streptococci were tested for haemolytic property in vitro as described by Lyall. Hiss serum water and media containing 1 per cent salicin, raffinose, inulin and mannite, were used to determine the fermentative action. Agglutination and protection tests were performed with the pneumococci to determine type.

Gram negative cocci. Several organisms of chromogenic type resembling micrococcus catarrhalis and micrococcus pharyngeus siccus are grouped under this head. As they were not found in large numbers,

TABLE 2

Streptococcus-pneumococcus group

STRAIN	SALICIN	RAFFINOSE	MANNITE	INULIN	HAEMOLYSIS	BILE	REMARKS
1/M	+	0	+	0	++++	0	No capsule
1/3	0	0	0	0	MHB*	0	
2/1	0	0	0	0	MHB*	0	
2/M	+	0	0	0	0	0	No capsule, slight clear zone beneath colony on plate, streptococcus mucosus.
3/M	+	+	+	+	MHB*	+	Capsule, pneumococcus III.
3/4	0	+	0	0	MHB*	0	
3/5	0	0	+	+	MHB*	0	1 cc. broth culture non-pathogenic for mouse, no capsule
4/3	+	0	0	0	0	0	
4/4	+	0	0	0	++++	0	
5/2	+	0	+	+	MHB*	0	No capsule.
6/4	0	0	+	0	MHB*	0	
7/M	+	+	+	+	MHB*	+	Capsule pneumococcus IV
8/M	+	+	+	+	MHB*	+	Capsule pneumococcus II
8/1	+	0	0	0	++	0	No capsule streptococcus mucosus

* MHB methhaemoglobin production without haemolysis.

no detailed identification was undertaken beyond some sugar fermentations. These are presented in the following table.

TABLE 3

Gram negative cocci

STRAIN	TYPE OF COLONY	DEXTROSE	MALTOSE	LACTOSE	SACCHAROSE	CORRESPONDS TO:
2/2	White, moist	+	+	+	Alkaline	
3/2	White, dry	+	+	0	+	Micrococcus pharyngeus siccus
3/3	Yellow, dry	+	acid	0	+	Chromogenic I. (Elser and Huntoon)
4/1	Yellow, dry	+	+	0	Acid	Chromogenic I. (Elser and Huntoon)
5/3	Yellow, dry	+	+	0	Acid	Chromogenic I. (Elser and Huntoon)
6/3	Yellow, dry	+	+	0	Acid	Chromogenic I. (Elser and Huntoon)
7/3	Yellow, dry	+	+	0	Acid	Chromogenic I. (Elser and Huntoon)
8/3	Yellow, dry	+	+	0	Very slightly acid	Chromogenic I. (Elser and Huntoon)

The staphylococci were tested for their reactions on litmus milk, liquefaction of gelatine and their pathogenicity. Table IV presents these reactions.

TABLE 4

Staphylococci

STRAIN	COLOR	LITMUS MILK	GELATIN	
1/2	Yellow	0 Alkaline	0	
2/5	White	+	0	1 cc. broth culture non-pathogenic for mouse.
4/6	White	0		
6/2	White	+		1 cc. broth culture non-pathogenic for mouse.
7/4	White	Slightly acid		1 cc. broth culture non-pathogenic for mouse.
8/2	Yellow	+ peptonized	+	1 cc. broth culture non-pathogenic for mouse.
1/4	White	0	+	

Length of observations. Subsequent to the first examination the sputum was examined bacteriologically once a month to observe the persistence of the haemoglobinophilic organisms. They persisted continually and were never lost during the period of observation.

In January, 1916, a detailed bacteriological study was made of those patients included in Table 1, who still remained in the hospital and the following organisms were obtained.

TABLE 5

CASE NO.	BACILLUS INFLUENZAE	STREPTOCOCCUS MUCOSUS	PNEUMOMUCOSUS	STREPTOCOCCUS HAEMOLYTICUS	STREPTOCOCCUS NON-HAEMOLYTICUS	GRAM NEGATIVE COCCI	STAPHYLOCOCCUS ALBUS	STAPHYLOCOCCUS AUREUS	DIPHTHEROID	PNEUMOCOCCUS
2	2	1	—	—	—	—	3	—	—	—
4	1	—	—	—	2	—	3	—	—	—
6	2	—	—	—	1	3	4	—	—	—
8	1	—	—	2	3	—	—	—	—	—
9*	1	—	—	—	—	2	—	—	—	—

* Case 9, admitted in December 1915, was not included in table 1. Cases 1, 3 and 5 left the hospital before this examination.

Danger as carriers. To compare findings with those in patients with positive tuberculous sputums, twenty-eight such cases were studied. Twenty-five of these had tubercle bacilli in the sputum, while three were clinically tuberculous, but without tubercle bacilli in the sputum. Most of the cases were selected because of their proximity to the above chronic non-tuberculous cases, in order to observe the occurrence of

haemoglobinophilic organisms in their sputum and to determine the possible transmission of influenza bacilli of the type here observed to the tuberculous in their immediate vicinity. The complete sputum procedure was repeated twice in two months in these twenty-eight cases. More than one hundred and eighty strains of various organisms were isolated from the twenty-eight cases without encountering the bacillus influenzae once. Two strains of small Gram negative bacilli morphologically resembling the bacillus influenzae were isolated; one from a case of advanced tuberculosis; another from a case of moderately advanced tuberculosis. These organisms upon subsequent transplants grew on ascitic agar, and can therefore be discarded as not being true influenzae bacilli.

DISCUSSION

From Table 1 it will be observed that Bacillus influenzae was isolated in seven out of eight cases. In four of these seven it was by far the predominating organism, and second in point of frequency in the other three. In one case (No. 4) Bacillus influenzae predominated to such an extent as to be in almost pure culture. Types of the streptococcus predominated in two cases and an apparently inconsequent Gram negative bacillus in one case. The influenza bacilli here isolated seemed of low virulence, and apparently are not transmitted to contact cases of tuberculosis in their environment. Perhaps the usual use of the gauze handkerchief and sputum box is enough to prevent this. At least it is determined that patients carrying these types of bacillus influenzae were not a source of danger to the tuberculous patients. However the persistence of the organism in the sputum places these patients in a carrier group. There may be some etiological connection between the bacillus influenzae and the base lesion in the lung. Other organisms may occur predominantly, however, and persist to a like extent.

CONCLUSIONS

1. The diagnostic value of examination in the inverted position is emphasized to localize physical signs in cases of suspected base lesion with few or no signs on ordinary examination.

2. The inverted position for pulmonary toilet, four times a day for fifteen minutes or more, at the periods most likely to remove sputum retentions of as little as 1 to 3 cc., is of great therapeutic benefit.

3. Bacillus influenzae is not common in the sputa of tuberculous patients in this hospital, even in those in contact with bacillus influenzae carriers. The dissemination therefore of bacillus influenzae seems to be prevented by the usual cough-sputum prophylaxis of tuberculous patients.

4. Bacillus influenzae is very frequently encountered in the sputa of "chronic non-tuberculous lung infection." It is found more frequently than any other type and is usually of low pathogenicity for laboratory animals.

5. The etiological significance of the common secondary microörganisms in chronic non-tuberculous lung infection is suggested by their predominance and persistence.

SEROLOGICAL STUDIES IN TUBERCULOSIS

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SYNOPSIS

I. Complement fixation in tuberculosis
  (a) Antigens
  (b) Haemolytic system
  (c) Material used
  (d) Technic, the test
  (e) Clinical data
II. Animal experiments
III. The Wassermann reaction in tuberculosis
IV. Discussion and conclusion

Infection as explained today is a contest between two antagonistic forces, the invading organism and the defensive bodies of the host. If the Ehrlich side-chain theory is accepted, then we expect that when the organism enters the body, the cells are called upon to protect against it. This protection is carried on by the antibodies which are formed and given off by the cells. The outcome of this struggle depends chiefly on the resourcefulness of both forces, and it may lead either to recovery or clinical disease. In order to comprehend this phenomenon we must bear in mind Weigert's law, "that the regeneration not only compensates the defect but over-compensates it." At the beginning of this struggle the resourcefulness must be at its highest efficiency, the organisms exercising strong biological activities, and on the other hand the cells by some process trying to overcome the invading organisms or their product. During this struggle it is possible today to demonstrate evidence of these activities with the aid of the complement fixation reaction.

Early workers in this field failed to obtain results which could justify the adaptation of this biological test in tuberculosis. The low percentage of positive reactions in early cases, the positive reactions in a good many arrested cases, and the occasional non-specific reactions of normal sera seem to have had some bearing on the test, so it was soon abandoned. However, in the last few years, study of it has been re-

newed with much vigor, for which the French investigators are responsible. By a better working knowledge and with the introduction of some new antigens the results have been surprising. The positive reaction obtained in early active cases and the negative reaction in apparently cured cases justify the deduction that after a better understanding and interpretation the test may be of some value in tuberculosis.

Complement fixation in tuberculosis has been an important factor to many investigators. Clinicians of today are not wholly satisfied with the physical and X-ray findings. The leading question after the anatomical diagnosis is, what about the activity of the disease as interpreted by such findings? Has the patient in question active or arrested tuberculosis? Clinicians also tell us that the verdict of "apparently cured" must be accompanied by a record free from symptoms for at least two years. This almost empirical observation of clinicians runs very closely parallel with the serological findings.

We shall not make an attempt to review the recent literature on this subject. The reader is referred to the splendid papers and reviews of Stimson, Bronfenbrenner, Craig and Miller, which have appeared in the last few years. The results obtained by the authors mentioned seem to us to uphold the view that the complement fixation test, as applied in tuberculosis, is more nearly specific than the Wassermann test. It must be remembered that the clinician should not expect the laboratory man to make the diagnosis for him but with the serological test to help him make the diagnosis. The main question now concerns "crossed" fixation in the luetic cases. Later in our paper we will attempt to express our views on these cross fixations. This test offers an opportunity to study the clinical course of an active case, and it eventually may lead to the better understanding of some obscure questions of immunity in tuberculosis. Animal experimentation, however, is much more important than the study of clinical cases, and only through this avenue is the truth of immunity likely to be revealed. This test offers a great opportunity to the experimenter to study the appearance and the disappearance of the antibodies in the blood of experimental animals.

ORIGINAL INVESTIGATION

At the beginning of this investigation, the problem was to study the values of different antigens with the object of finding one which might help us to separate the active from the arrested tuberculous cases, and

one which would give us a high percentage of positive reactions in very early active cases. In a period of almost three years we have had the opportunity to study many antigens used by the early investigators, and every new one appearing in the current medical literature. The following were the antigens studied by us: Radcliffe's, Craig's, Miller's, and some twenty modifications of these. There were a good many advantages as well as disadvantages with all preparations. Practically all have some antigenic properties, and our own was not an exception. There is still much room for improvement.

Several years ago we described a potato broth as culture media for the tubercle bacilli. Later it was suggested to us that the filtrate of such cultures, on account of their low content of foreign proteins, might be an ideal antigen for the complement fixation test, and we adopted it as our first standard.

After a careful study of several hundred cases it did not come up to our expectation, because in about 15 per cent of known positive active cases we obtained a negative reaction. An alkaline extraction of tubercle bacilli furnished an antigen that proved to fill the gap. The next step was to devise a lipoid antigen. Ether, ethyl alcohol, benzol, xylol, toluol, chloroform and methyl alcohol were used for the extraction of lipoids from the tubercle bacilli. The methyl alcohol extract proved to be the strongest in its antigenic properties, and was introduced in our routine work.

Antigen No. 1 (P. F.) was polyvalent. It was made from six strains of human and one of bovine tubercle bacilli, grown separately on potato broth.[1] After six weeks the broth was filtered very carefully through several thicknesses of filter paper. Care was taken not to contaminate the filtrate. It was found that preservatives will in time render this filtrate anticomplementary, so neither phenols nor lysols were added. With experience one can invariably tell whether the filtrate is of the proper strength and antigenic properties. The indication to be noted is the changing of the color of the potato broth from dark brown to a golden yellow after the tubercle bacilli have been grown on it. This

[1] This broth is prepared as follows: 500 grams of grated potato are infused in 1000 cc. of distilled water for twenty-four hours in the ice box. At the end of this time the infusion is filtered from the pulp through gauze, titrated, and the reaction adjusted to about 1 per cent acid. The filtrate thus obtained is heated in the autoclave at 15 pounds pressure, for one-half hour, then filtered through filter paper. This clear brown fluid is again titrated, and the reaction adjusted to 0.5 per cent acid. Glycerin is then added to make a 4 per cent solution, 50 cc. of broth is put into a 250 cc. flat bottle, and sterilized by fractional sterilization.

antigen was then put in small ampules containing 2 cc. sealed and stored in the ice box. An antigen thus prepared and stored has been kept in our possession as long as two years without losing its antigenic properties.

Antigen No. 2. Two hundred and fifty milligrams of dried, pulverized tubercle bacilli were extracted with 50 cc. of 1 per cent sodium hydrate in water. The extraction was carried on at 38°C. for from five to ten days. At the end of that time this extract was neutralized with normal hydrochloric acid, and was ready for use. Care was taken during the process of neutralization not to carry it beyond the neutral point. If by an error it passed the neutral point such antigen was discarded. It is well to remember that the neutralization is the most important step in the preparation of this antigen. This antigen also was found to be very stable.

Antigen No. 3. Two hundred and fifty milligrams of dried, pulverized tubercle bacilli were extracted with 50 cc. of methyl alcohol (Merck's reagent) at 38°C. for from five to ten days. At the end of that time it was well corked and set aside in a dark place at room temperature. After several weeks the clear supernatant fluid was pipetted off, and was ready for use. It is advisable to store this antigen in small ampules or small bottles because of its being prepared with methyl alcohol, which is very hydroscopic. A small amount of moisture will, in time, render it anticomplementary, and will reduce its antigenic properties. When used it is diluted with physiological salt solution.

DISCUSSION OF ANTIGENS

Antigen No. 1 was polyvalent. When a monovalent antigen was used, we got a positive reaction in only about 30 per cent of sera from clinically active tuberculosis. On the other hand, if several more strains were used, we got positive reactions in a much larger percentage. This antigen very likely contains autolytic substances from the tubercle bacilli. After the organism has been grown it must be filtered through filter paper. If it is filtered through a Berkefeld filter, the filtrate contains a very small amount of antigenic properties. There is no doubt that when filtered through filter paper some tubercle bacilli are also carried through, but they are very seldom demonstrated in the filtrate, and in only one instance have we been able to infect guinea pigs; so it is doubtful if the antigenic properties of the filtrate are due to the few tubercle bacilli which may have passed through the filter paper. It may

be possible that some colloidal substances are responsible for the strength of this filtrate which passes through filter paper, and that it is held back when a Berkefeld is used. We may obtain apparently as good results if we use ordinary beef broth cultures. If it is filtered through a Berkefeld filter the filtrate contains no appreciable antigenic properties, but when these same cultures are filtered through several thicknesses of filter paper we get a filtrate with considerable antigenic power.

Antigen No. 2. We took 250 mgms. of dried, pulverized tubercle bacilli and extracted them in 50 cc. of 0.85 per cent sodium chloride solution at 38°C. for five to ten days, and we got no antigenic properties of great value. The same result was also obtained when ordinary bacillus emulsion was used as antigen. There is no question in our mind but that with sodium hydrate we extract some antigenic substances which cannot be extracted with sodium chloride. This sodium hydrate extract is a very important and reliable antigen. However, its preparation is very delicate, as already stated, and much care must be taken when neutralized that it is not carried beyond the neutral point. At the beginning of our investigation we used seven strains of human and bovine tubercle bacilli in this extraction. After studying the extraction of different types of acid-fast organisms like the smegma bacillus, avian tubercle bacillus and a number of types of human and bovine tubercle bacilli, we came to the conclusion that all types of ac d-fast organisms have similar antigenic properties if thus treated. Recently we have used a monovalent antigen which proved of equal value to the polyvalent one. Another factor must be considered in the preparation of this antigen; that is, that pulverized tubercle bacilli will give us a better antigen than the intact tubercle bacilli.

Antigen No. 3. This antigen was not so important from the "active-arrested" standpoint. Using this antigen we may demonstrate antibodies for a long time after the patient has been free from symptoms. We have demonstrated the existence of such antibodies as long as two years after the disease has been arrested. It is hoped, however, that this antigen may prove to be of some value in the prognosis. Such an extraction, without doubt, contains large quantities of lipoids. The question arises, will such extraction give cross fixation with luetic sera? From an experimental standpoint this antigen has proved to be of extreme interest, and, under the rabbit experiment, we will describe our reactions with sensitized and nonsensitized rabbits.

HAEMOLYTIC SYSTEM

Amboceptor. In practically all of the tests given in this paper the haemolytic system was antisheep, and was obtained as follows: Rabbits were injected on the first, third and fifth days with 50 per cent of carefully washed sheeps' red cells in amounts of 2 cc., 3 cc., and 4 cc., respectively. On the eighth day they were bled from the carotid artery and the serum, after inactivation, was stored in small ampules in the ice box. A haemolytic amboceptor obtained by this method proved to be very efficient and of very high titre.

Sheeps' red cells were a 5 per cent suspension of the concentrated red cells in 0.85 per cent sodium chloride solution.

The complement. Ten per cent of fresh guinea pig serum was used in all of our tests. The method of storing a pool of guinea pig serum with the sodium chloride did not prove very satisfactory.

Patients' sera. The patients' sera were inactivated in a water bath for one-half hour at 56°C. In about one hundred cases the sera were not inactivated. Various dilutions of the active sera were used. As these sera very often gave a nonspecific reaction, very likely due to some proteotropic reaction, as pointed out by Noguchi, the method was discarded.

The complement was very carefully titrated, and a double unit of complement with a double unit of rabbit's amboceptor used in the test. The amount of the antigen used in every test was one-fourth of the anticomplementary titre. In titrating the antigens it was found that a normal serum did not fix the complement in 0.8 cc. dilution while a known positive serum fixed it at 0.05 cc. dilution.

The test. One-tenth of a cubic centimeter of inactivated serum, one-fourth of anticomplementary dose of antigen, two units of 10 per cent complement and sufficient 0.85 per cent sodium chloride solution to make up a total volume of 2 cc. when we added the haemolytic system were shaken well and incubated at 38°C. for one and one-half hours. It will be noticed that the incubation of our bacteriolytic system was one and one-half hours. Some objection may be raised as to the thermolability of the complement. We do not agree with some investigators that the complement spontaneously loses its power by incubating at 38°C. for an hour. We have repeatedly demonstrated that after as long as six hours incubation at this temperature the strength is not diminished. Patients' sera were controlled as to their anticomplementary properties.

This alsoserved as the control for natural antisheep amboceptor. Antigen control was double the amount used in the test. At the end of one and one-half hours' incubation 0.5 cc. of 5 per cent red cells were added and the control for the haemolytic system and the anticomplementary tubes were returned to the water bath for fifteen minutes. After fifteen minutes of incubation the rabbit amboceptor was added proportionately. It has been our observation that in about 60 per cent of all sera we can demonstrate natural antisheep amboceptor, a fact which has been observed by a good many investigators. How much this antisheep amboceptor interferes with the reaction we are not able to state. It is a well known fact that natural antisheep amboceptor has also been demonstrated in guinea pig and rabbit sera.

The clinical aspect of this paper is based on results obtained with the sera of more than seven hundred individuals, the majority of whom were Sanatorium patients. Fifteen hundred tests were made. We had some cases from private sources, whose sera were sent to the laboratory in numerical order, and only in a few instances were the names given before the tests were made. The Sanatorium sera were taken by one of the assistant resident physicians and not by the author. This was done so that the results could not be biased. After the tests were made the results were compared with the physical and X-ray findings and then recorded on the cards.

To eliminate the possibility of the interference of the diagnostic skin test, we had the complement fixation done prior to the tuberculin skin test. So far we may safely say that intradermic skin tests have little or no influence on the complement fixation. The results of this test may be summarized in the following table:

TABLE 1

	CASES	NUMBER OF TESTS	POSITIVE COMPLEMENT FIXATION	NEGATIVE COMPLEMENT FIXATION
Clinically active tuberculosis	212	617	199	13
Quiescent tuberculosis	158	301	89	69
Apparently cured more than two years	58	193	5	53
Normals	78	96	3	75*
Suspected	166	267	65	101
Other diseases	41	81	6	35

* Seven of these were one plus (+), which we have put in the negative column.

We have made an attempt to group the cases presented in our table according to the classification of the physical examinations (that is, incipient, moderately advanced and advanced), but this proved to be so little value that it was abandoned. At first glance it will be noticed that we have performed more than one test on each patient. In some cases we made two, while in others as many as twelve tests were made. The object was to see how the complement fixation test would correlate with the clinical course of the disease. It was invariably found that as the patient improved the complement fixation test became weaker and weaker until finally the test was completely negative. This, in time, may prove of great value to the clinician as to prognosis, and eventually it may lead to some better understanding of individual cases. The disappearance of the antibodies from the blood stream of a patient previously giving a positive fixation does not follow any definite rule. In some cases the test becomes negative much sooner than in others.

In the first group in table 1 (Active tuberculosis), we note cases w'th active symptoms of the disease. In some cases tubercle bacilli were never demonstrated, but in a majority they were present. The high percentage of positive findings speaks well for the reliability of the test.

We are reluctant to say very much about the second group (Quiescent). It is a group regarding which clinicians will always disagree: A case may give a positive fixation today and again in a few days give a negative fixation, and *vice versa*. Mild physical exercise may provoke the appearance of a positive reaction. According to the classification of the National Association, the sputum of this class may be positive or negative. These are the cases lying on the border line between the group of active and apparently cured. A very interesting point which we would like to point out is that eighty-nine of the hundred and fifty-eight cases in this group had positive tubercle bacilli in the sputum. Eighty-three of the eighty-nine with positive sputum gave a positive complement fixation, a fact which confirms the clinical findings.

The third group (Apparently cured) is one of the most interesting. All fifty-eight had had known positive tuberculosis, and at the time of the test have been free of symptoms for more than two years. All but five gave negative complement fixations.

The fourth group (Normal) is of some interest. The positive reaction in the three cases might possibly be exp'ained by their constant association with tuberculous patients although no clinical tuberculosis was present.

The fifth group (Suspected) is a very puzzling one. In some of these cases physical examinations were positive, while in others the X-ray was positive and the physical examination negative. In this class we had patients always with some symptoms of tuberculosis, either loss of weight, rapid pulse or some slight fever. When the complement fixation test was made, none had tubercle bacilli in the sputum. Some of these cases later developed definite clinical tuberculosis and in some instances the tubercle bacilli appeared in the sputum. The intradermic tuberculin skin test was positive in all but one case which failed to react to 10 mgms. of tuberculin subcutaneously, while the complement fixation was repeatedly positive.

The sixth group (table 2) will explain itself. We merely want to call attention to the case V.–II at the bottom of the table. This was the only case which came to autopsy, and the complement fixation result could be verified by the postmortem examination.

Relation to tuberculin test. Attention should be directed to the correlation of the intradermic skin test to the complement fixation. The skin test and the complement fixation test, as we know, bring out two entirely different phenomena. The former deals very likely with cellular antibodies, while the latter demonstrates a strictly humoral phenomenon. In the early stages of the disease these two tests do not correlate, but as the patient becomes moribund they begin to run closely parallel. It is a well known fact that in such cases the skin test is very weak, and very often it may be entirely negative. Complement fixation was performed on a few such cases, and then proved to confirm the skin test.

As we have already stated, we expect a negative fixation where the disease is completely arrested. Over 50 per cent of the quiescent cases give us a positive reaction. In such a condition the interpretation may be offered that the clinical condition could not be recorded on a straight line; that is, one day, when the patient is free from symptoms, there will be no antibodies in the blood stream and thus complement fixation is negative, while on another day, after violent exercise or some other physical condition, we may get antibodies in the blood stream, which could be demonstrated by the complement fixation test. It must be remembered that one test is not sufficient for a final verdict. Only after repeated negative examinations may we safely say that the case is apparently arrested or apparently cured.

TABLE 2

Other diseases

ORIGINAL NUMBER	COMPLEMENT FIXATION FOR TUBERCULOSIS	DISEASE	REMARKS
39	+++	Asthma	Father tuberculous
51	0	Lung abscess	
62	0	Lung tumor	
63	0	Kidney in question	
71	0	Chronic bronchitis	
117	+++	Asthma	
121	++++	Leukaemia	Wife tuberculous
170	+++	Chronic bronchitis	Father and two sisters tuberculous
173	0	Influenza	
101	0	Lobar pneumonia	
215a	++	Asthma, bronchitis	
219	0	Lung abscess	
247	0	Emphysema, asthma	
268	0	Lung tumor	
273	0	Chronic bronchitis	
241	0	Lung abscess	
25	0	Kidney in question	
26	0	B. coli infection	
36	0	Neurasthenia	
204	0	Influenza	
215	0	Suspected hyperthyroidism	
238	0	Hay fever	
240	0	Tracheitis	
249	0	Hysteria	
253	0	Chronic bronchitis	
281	0	Enlarged tonsils	
22b	0	Bronchiectasis	
118	0	Malignancy	
L.B.	0	Leutic	
1c	0	Malignancy	
2c	0	Malignancy	
4c	0	Typhoid fever	
5c	0	Lobar pneumonia	
8c	0	Lues	
A. A. B.	0	Lues	
Cas. T.	0	Malignancy	
M. T.	0	Bronchiectasis	
V.–I	0	Malignancy	
V.–II	++++	Typhoid fever	Autopsy, recent tuberculosis
V.–III	0	Typhoid fever	
V.–VI	0	Malignancy	

Every patient admitted to the Sanatorium was given the following tests: first, complement fixation; second, intradermic skin test; third, X-ray examination; and fourth, physical examination. If there was any doubt as to the existence of tuberculosis in any patient, he was also given the subcutaneous diagnostic tuberculin test. A majority of the cases respond to such a test, with considerable variation in the severity of the reaction; that is, a mild focal reaction or a general reaction with high temperature. At the height of the reaction, we find that the blood will give a positive complement fixation, and râles may appear. If we examine the patient in question a few days after such a general tuberculin reaction has subsided, we find the blood will give a negative reaction, and upon examination the râles have disappeared. Whether the antibodies demonstrated after tuberculin reaction are antituberculin antibodies or antibodies due to the stirring up of the old focus, we cannot at present definitely say.

There are some other conditions which may provoke the appearance of a positive fixation where it has been negative. An apparently arrested case giving a negative complement fixation will, during a cold, give a positive complement fixation. This, however, will not happen with a perfectly normal individual. The explanation may be offered that, during such a time, the resistance is lowered and the preexisting tuberculosis again resumes an active stage for only a short time. As soon as the cold subsides, the blood again becomes negative.

EXPERIMENTAL DATA

An attempt was made to study the meaning of some of these reactions based on experimental evidence. These experiments were carried out on guinea pigs, rabbits and a cow.

Guinea pig experiments. If a guinea pig is inoculated with a virulent strain of tubercle bacilli and the blood subsequently is studied day after day, we may demonstrate complement fixing antibodies on the fifth or sixth day. The antibodies may be demonstrated as long as two weeks after the inoculation, and from that time on they gradually disappear from the blood stream, and in about three weeks can no longer be demonstrated.

Now, on the other hand, if we inoculate a guinea pig with a comparatively avirulent type of tubercle bacilli, like R_1, which produces only a localized tuberculosis we are able to demonstrate antibodies for a long

time. We may recall just for a moment the work of Bordet and Gengou in 1903, who when working on this reaction failed to get a positive reaction with the serum of guinea pigs previously inoculated with virulent human tubercle bacilli. These authors, however, were able to demonstrate the sensitizers or complement fixing antibodies in the sera of guinea pigs previously inoculated with avian tubercle bacilli, to which organisms, as we all know, they have a relative immunity.

The explanation may be offered that in guinea pigs inoculated with virulent human tubercle bacilli, we have a stimulation of the cells' bacteriophilic receptors (haptophoric receptors) and the fate of the infected organism depends on the amount of bacterial protoplasm which has become converted into toxic bodies. The activities of the antibodies in such a case are relatively low, so that the toxic substances formed are not rapidly broken down to non-toxic ones, and thus they rapidly accumulate. The rate of activity of the cells for producing such antibodies is gradually diminished, and the antibodies are outnumbered by the units of toxic substances, and the result is active progressive tuberculosis. In this state the antibodies no longer could be demonstrated by the complement fixation test. In cases where an avirulent strain of tubercle bacilli is used, the bacterial protoplasm is rapidly degraded beyond the toxic stage by the activities of the antibodies. The bacterial protoplasm is rapidly absorbed in such a state, and this results in the accumulation of the antibodies, which can readily be demonstrated by the complement fixation test.

Rabbit experiments. It is a well known fact that immunity to tuberculosis depends chiefly on a preexisting focus. Dr. Trudeau was one of the first to demonstrate this fact in case of rabbits. When rabbits are inoculated with human tubercle bacilli, to which they are relatively immune, it will be found that after a second inoculation with bovine tubercle bacilli they will outlive the control animals. The explanation to this may be that the preexisting focus has established a relative immunity to bovine tubercle bacilli, to which they invariably succumb. In the last few years this problem has been extensively studied in the Saranac Laboratory, which thus offered us an opportunity to study the blood of such treated animals. It must be remembered that rabbits are not ideal animals for such experimentation. Occasionally we got a very weak nonspecific fixation which, recently, we have well controlled.

In table 3, we have presented the experimental data of some of our animals. In studying this table we will see that even six days after the

TABLE 3

Rabbit experiments

NUMBER OF EXPERIMENT	TEST OF BLOOD AFTER SECOND INOCULATION	PRIMARY INOCULATION, HUMAN TUBERCLE BACILLI	SECOND INOCCULATION, BOVINE TUBERCLE BACILLI	TUBERCULIN REACTION	POTATO FILTRATE	SODIUM HYDRATE EXTRACT	METHYL ALCOHOL EXTRACT
	days	*subcutaneous*	*subcutaneous*				
86	6	H^{37}	B_1		++++	++++	++++
87	8		B_1		++++	++++	0
88	8	H^{37}	B_1	+++	++++	++++	++++
93	11		B_1		++++	++++	0
94	11	H^{37}	B_1	++	++++	++++	++++
95	15		B_1		0	0	0
96	15	H^{37}	B_1	+++	++++	++++	++++
97	18		B_1		++++	++++	0
98	18	H^{37}	B_1	++	++++	++++	++++
99	23		B_1		++++	++++	0
100	23	H^{37}	B_1	+++	++++	++++	++++
101	28		B_1		++++	++++	0
102	28	H^{37}	B_1	+++	++++	++++	++++
103	36		B_1		++++	++++	0
104	36	H^{37}	B_1	++++	++++	++++	++++
106	46	H^{37}	B_1	0	++++	++++	0
106	53	H^{37}	B_1	0	++++	++++	0
107	46		B_1		++++	++++	++++
107	57		B_1		++++	++++	++++
108	46	H^{37}	B_1	+++	++++	++++	++++
108	53	H^{37}	B_1	+++	++++	++++	0
110	46	H^{37}	B_1	0	++++	++++	0
110	62	H^{37}	B_1	0	++	++	+++

second infection we will get a four plus positive complement fixation test in the treated as in the control animals to our two first antigens, that is potato filtrate and sodium hydrate extract. If we look in the last column in this table we will see that only the treated animals have given us positive complement fixation with methyl alcohol antigen. These striking results have led us to a further experiment on a more extensive scale, the results of which we expect to publish soon. Perhaps an explanation of the experiment is not out of place. We have taken rabbits 86, 88, 94, etc., all even numbers, and inoculated them subcutaneously with human tubercle bacilli. Three weeks later the skin test was given, and after the skin test a subcutaneous inoculation of bovine tubercle bacilli was given to the previously treated animals as well as to the controls. For each treated animal a control was inoculated, so that the experiment might be well controlled. The rabbits

were either killed or bled at different intervals. It will be noticed that approximately every week the blood was drawn and complement fixation done. We want to call particular attention to rabbit 106. This rabbit was inoculated with human tubercle bacilli, but it failed to give us a tuberculin skin reaction as the others have. According to the other treated rabbits, we should expect a positive complement fixation with the methyl alcohol extract, but, as seen from the table, we did not get a positive reaction. Is it possible that our sensitizing dose was too small? Rabbit 107 is also very interesting. It gave strong positive complement fixation with methyl alcohol extract when it was not expected. This rabbit outlived all other controls. (Is it possible that rabbit 107 received a relatively smaller quantity of bovine tubercle bacilli, and consequently immunized itself against its own dose?) We cannot at present definitely answer the unexpected reaction with rabbits 106 and 107, but further experiments may throw some light on these reactions.

Cow experiments. Last spring we obtained, for the purpose of doing some serological experiments, a tuberculous cow condemned by the State officials. The animal reacted to the official State tuberculin test, with high fever and loss of appetite, as may be seen in the following table:

TABLE 4

March 15, 1916		*March 16, 1916*	
Temperature before injection		Temperature after injection	
9 a.m.	102.0°	10 p.m.	101.8°
12 m.	101.0°	12 p.m.	102.4°
2 p.m.	101.2°	2 a.m.	104.0°
4 p.m.	101.6°	4 a.m.	105.0°
At 4 p.m., March 15, 1.5 cc. of concentrated tuberculin was injected subcutaneously. Six hours after the injection the temperature was taken, and every two hours thereafter until 4 p.m. the following day. There was a maximum variation of 4°C. in the eighteen hours.		6 a.m.	105.0°
		8 a.m.	105.6°
		10 a.m.	106.0°
		12 m.	105.0°
		2 p.m.	105.8°
		4 p.m.	105.6°

Complement fixation at the time of the reaction was four plus, with all of the antigens. An attempt was then made to raise the titre of these antibodies, and so we injected her intravenously with approximately twenty milligrams of bacillus emulsion every week. Every injection of antigen was followed by general tuberculin reactions, with high fever and loss of appetite, which always subsided in about forty-

eight hours. After eleven injections the treatment was stopped. At the time of the test the titre of the antibodies was as high as one to five thousand. Five months later we tested the blood of the cow. To our surprise, we got a negative complement fixation with the three antigens, and the cow failed to react to 1.5 cc. of concentrated old tuberculin subcutaneously. It was then suggested that a tuberculin intravenous injection be tried. Five thousand anticomplementary units of Sodium hydrate antigen were injected. Again, as with the subcutaneous tests, the reaction was negative: no fever and general condition good. A week later we injected this cow with 10,000 units of the same antigen, and we have continued to do this for several months in the hope of raising the titre of the antibodies. In no instance was any fever demonstrated after the injection of the antigens, while the antibodies were increasing and we have at present fairly strong complement fixing antibodies.

The above experiments (with guinea pigs, rabbits and the cow) tend to show us that we can demonstrate experimentally complement fixing antibodies in animals. All this offers to experimenter an opportunity to study much better, in animals, the humoral side of immunity.

The question may be asked: Do these antibodies, present in the experimental animals and demonstrated by the complement fixation test play any important part in immunity? In other words, are they immune bodies? This is the question to which an answer must be reserved on account of the lack of experimental evidence.

WASSERMANN REACTION

We have taken for granted that in the Wassermann reaction we have a specific diagnostic test for syphilis. It is a well established fact among investigators in this particular line that the Wassermann reaction is nothing but a lipotropic reaction and that if the specific organism of this disease is treponema pallida, which has been cultivated by Noguchi and others, then we should expect that the best results are to be obtained from an antigen prepared from the organism itself.

In the last few years we find many conflicting reports in the literature regarding this reaction, and particularly with reference to the observation of positive reactions among patients with tuberculosis. The most radical investigators in this field tell us that syphilis is not uncommon in tuberculosis.

Of the 297 cases studied by Bronfenbrenner 62 gave a positive com-

plement fixation for tuberculosis with the use of Besredka's antigen. Of these 62 positive cases, 31 also gave a positive Wassermann reaction. The author, however, does not mention the antigens used in the latter test.

Snow and Cooper were the first to call attention to the fact that about 31 per cent of tuberculous sera studied by them gave a positive Wassermann test with cholesterinized heart extract. They concluded that only the crude alcohol extract is reliable in the Wassermann test. McClure and Lott have also come to the conclusion, after extensive study, that cholesterinized heart extract is more sensitive than a crude alcohol one, but they emphasize the fact that the former antigen is less specific than the latter from a diagnostic standpoint in syphilis. More recently Smith and McNeal have come to practically the same conclusion as the above mentioned authors, and they also stress the fact that a positive Wassermann reaction with cholesterinized antigen is not trustworthy.

In a good many cases of laryngeal tuberculosis with no evidence of lues, some investigators have reported positive Wassermann reactions, but in this latter group we have no report as to the antigen used in the test. Our results with laryngeal tuberculosis uphold the findings of the above investigators.

During the last few years opportunity has been offered us to carry this particular line of investigation further. When we began the study, the object was to find out how often positive Wassermann reactions could be demonstrated among patients with tuberculosis. Three antigens were used in our investigations; namely, cholesterinized beef heart extract, crude alcohol beef heart extract and acetone precipitate from the crude alcoholic beef heart extract, according to the method of Thiele and Embleton. The cholesterin used in cholesterinized antigen was prepared by us from the gall stones of a tuberculous patient. As the work progressed, on tabulating about one hundred cases, we thought that something must be wrong with the cholesterinized antigen because as many as thirty tuberculous patients gave a positive Wassermann test with this antigen, while with the crude alcohol and acetone precipitate antigen results were negative. To check up results obtained with the cholesterinized antigen, we used two new lots of cholesterin, one from Merck and one from Eimer and Amend. The results obtained by the use of the latter two samples of cholesterin in our antigens were approximately the same as with the first preparation, so we continued to carry these antigens along with the others in the Wassermann test.

The test for lues was run parallel with the complement fixation test for tuberculosis on every case that came to the institution to see how many cases will give positive Wassermann reactions with the cholesterinized antigen and how many with the crude alcohol and acetone precipitate.

A study was undertaken to see what would be the results if cholesterin alone is used as an antigen. Four-tenths of a gram of cholesterin was dissolved in 10 cc. of absolute alcohol and left in the incubator at 38°C. for twenty-four hours. At the end of this time it was diluted with salt solution in the proportion of one to ten, and various amounts of this cholesterin and alcohol preparation were titrated in the usual way. After the proper titre was determined, this preparation was carried along with the other Wassermann antigens. Positive reaction was obtained with the cholesterin-alcohol preparation in about 25 per cent of a series of over two hundred patients' sera.

The results obtained may be summarized as follows: Of the 376 cases with a positive complement fixation for tuberculosis, 82 gave a positive Wassermann reaction with cholesterinized heart extract, while only 9 gave a positive reaction to alcoholic and acetone precipitate antigen. Every one of these 9 cases gave a positive history of lues.

SUMMARY AND CONCLUSION

We have used three antigens to study complement fixation in tuberculosis. In potato filtrate and sodium hydrate extract we have very good antigens. Neither of these alone is sufficient. We may get positive reaction with one and not the other, and *vice versa*. A positive reaction with either means, very likely, active disease. Our experience with all antigens today is that not a single preparation answers as a "shotgun" preparation, and that more than one antigen must be used. If the cases from a clinical standpoint are not running a similar course, we do not see why they should be alike from a serological point of view. It is very likely that there is a multiplicity of antibodies, and if there is a multiplicity of antibodies there must be partial antigens.

The test is very simple and can easily be carried parallel with the Wassermann test. A sanatorium is the only place where the sera can be studied for a long period of time, and this is necessary before it is adopted as a diagnostic test. In private practice it is as yet not practical, because we are not, at present, sure of the interpretation.

If we take the two important groups of cases, which from a clinical

standpoint are put in their respective classes, that is, the active and apparently cured, we find that the complement fixation is positive in a very large percentage of the active cases and the reverse with the apparently cured. From the above results it may be deduced that a positive reaction probably means active tuberculosis and a negative, inactive disease.

Quiescent cases are those lying on the border line between the active and the cured. Neither positive nor negative reaction means anything when the test is done only once. The blood of cases belonging in this class must be studied every month and then the findings may have some meaning. The suspected, normal and other disease groups must be studied extensively before we can draw any conclusions.

Animal experimentation, as we have stated elsewhere, is much more important at present than clinical study, and through this channel we may obtain definite conclusions.

In a patient with tuberculosis, a diagnosis of syphilis based on the Wassermann test, using only the cholesterinized heart extract antigen, is deceptive. Our results indicate that lues is not common in tuberculosis.

R_1 is a human tubercle bacillus culture, isolated by Dr. Trudeau about twenty-five years ago. It has lost much of its original virulence, and when inoculated into guinea pigs produces only localized tuberculosis.

H_{37} is a human tubercle bacillus culture which produces generalized tuberculosis in guinea pigs.

B_1 is a bovine tubercle bacillus culture, virulent for rabbits.

EDITORIAL

THE AMERICAN REVIEW OF TUBERCULOSIS

It is with no desire merely to add one more to the rapidly growing number of medical journals or to force for itself "a place in the sun" that THE AMERICAN REVIEW OF TUBERCULOSIS makes its bow to a patient medical public. The present venture is the culmination of many years' more or less prayerful discussion in the councils of the National Association for the Study and Prevention of Tuberculosis as to the necessity and desirability of a special journal on tuberculosis. Year after year there have been many arguments pro and con, but with the advance of time the demand for a journal has grown louder and louder while the voices of the timid have been gradually stilled.

Those whose daily lives are busied in work in tuberculosis are convinced that we are entering an era of discovery and of orientation in regard to the disease. Tuberculosis, it is true, has had its epochs in the past. The eighteen eighties was the decade of the bacillus, the eighteen nineties that of tuberculin, while the last decade has been noteworthy because the wheat of the two former eras has been separated from the chaff, and has been brought into harmony and coördination. We no longer look up the bacillus as the sole factor in the production of the disease tuberculosis. We no longer regard tuberculin either as a cure-all or as anathema. We have learned that besides a seed the disease tuberculosis requires a soil for its development, and once having realized this fact we have taken a tremendous step forward. We now appreciate that we must study not only the offending microörganism but also the smitten host, and must weigh and examine all the interactions between the two. We know also that by the study of tuberculin and its effects we are gradually gaining an insight into the most fundamental and far reaching problems that the disease presents for solution.

It is only within the last five or ten years that our knowledge of the relations of infection to disease has taken definite form and has become vulgarized. Years ago an elect few had a glimpse into the probability that to be a civilized human being was to be tuberculous and that only

a few of the myriads of the tuberculous ever developed tuberculosis. But at the time the facts were not at hand to warrant positive statement. Today they are. And if anyone doubts that we have learned much and have traveled a long way since 1905 let him read a work on tuberculosis of today and contrast the point of view with that held ten years ago. Or let him read the writings of Dr. Trudeau consecutively beginning about 1890 and ending in 1915. He will see how timidity of statement gradually hardens into positiveness and, here and there, evolves even into pregnant prediction as the hard won facts come in—all too slowly sometimes, yet uninterruptedly.

Our changing point of view requires that we undertake new studies and perhaps alter or supplement our method of attack. During the last fifteen years we have drifted far from the Cornet doctrine that we inhale infectious dust and soon thereafter fall ill or the Flügge dogma that we live in a world of noxious droplets from which there is no escape unless we cease our coughing, sneezing, laughing or loud talking. We now talk of preventing the development of tuberculosis by keeping under control old and long established benign tubercle. We study the infected individual and try to discover what it is that ripens old quiescent tubercle, how the germ gains entrance to the body, where it goes after it enters, what effects it produces immediately, how it spreads from place to place and what factors determine its ultimate effects. Moreover the discovery of salvarsan, a remedy for a kindred disease, and the theoretical studies that led to this discovery have stimulated a great deal of work in the search for a therapeutic agent against tuberculosis. And anyone who has lived through the last twenty years and has seen the vaunted cures come and disappear will affirm that never before has the quest for a cure for tuberculosis proceeded along such rational lines as now.

With the growing appreciation of the universality of tuberculous infection and increasing information of the factors that convert this infection into disease has come a stronger and stronger feeling that in the last analysis the practical fight against tuberculosis must be along broader lines than those which are purely medical. The social and economic side of the problem has demanded and has received an ever widening attention. Physicians have come to realize that it bulks large and is ever pressing.

For many years practically all of the money that was applied to the campaign against tuberculosis was directed to the establishment of

sanatoria for the sick. This was only natural before we recognized as we do today that most of us are potentially tuberculous and that relapse is as striking a feature of the disease as its tendency to arrest under the proper conditions. But as our realization of the limitations as well as the undoubted value of sanatorium treatment in its effect on the ultimate conquest of tuberculosis has taken definite form, we find that there is an increasing tendency to supplement this expenditure of money for sanatoria with grants to what may more properly be called the pure study of tuberculosis. The wonderful Phipps foundation at Philadelphia, the Patten grant at Evanston, the Trudeau foundation at Saranac Lake, the Dows foundation at the Johns Hopkins Hospital, and the Metropolitan Life Insurance Company's experiment at Framingham are all examples of this renewed interest in research in tuberculosis and promise ample dividends on the investment.

Because of this ever growing interest in tuberculosis work, because of these many activities that should have a converging focus, the National Association considers that the time is ripe to offer all who are interested a medium in which they can present their work and through which they can develop their views. A leading motive of the REVIEW will be to stimulate productiveness as well as to interest those men who though not directly concerned with tuberculosis are working in more or less related fields. The REVIEW goes to the medical public asking its support and welcoming any contribution that conveys a message from the field of tuberculosis, whether this message be culled from experimental work on animals or with the test tube, from clinical observation on the patient, from speculation on the sequence of cause and effect or from experience in the world at large. A. K. K.

MEDICAL NOTES, ABSTRACTS AND REVIEWS

It will be the eventual purpose of the REVIEW thoroughly to canvass all literature on tuberculosis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Abstract Editor, Dr. George Mannheimer, 41 West 51st Street, New York, N. Y. In the present number many of the abstracts have been taken from other medical publications, such as the Journal of the American Medical Association, the Medical Record, the New York Medical Journal, etc., to whom acknowledgment is due.

Fallacies About Tuberculosis.—The numerous fallacies with which tuberculosis is burdened have wrought great harm to both patients and profession. It is a common belief that the disease is transmitted from the sick to the well. Not every infection with bacilli causes the disease; if this were not so, over 90 per cent of humanity would be sick and succumb to the disease. It appears that infection alone is, as a rule, powerless to produce consumption; there must also be an organism which is peculiarly predisposed, though we are still in the dark as to the nature of this predisposition. The belief that a person may be infected several times with the virus of tuberculosis is also fallacious. Nearly all human beings living in civilized communities have been infected before adolescence; some have developed the disease but most have continued in good health and have become immune to further infection. It is a fact that hospital staffs in institutions harboring tuberculous patients do not suffer from tuberculosis more than others. Likewise, consumption in both husband and wife is exceedingly rare. Inasmuch as adults cannot be infected with tubercle bacilli, it is problematical whether the vigorous "follow-up" system practised by the health department in New York City is justified. If a tuberculous husband cannot infect his wife we may assuredly conclude that he cannot infect his neighbor in the factory. The decline in mortality is no evidence of the efficacy of the "campaign." The mortality began to decline before the campaign was inaugurated, and the decline has been observed in countries where no campaign has been waged. In some countries where the fight has been waged no decline has resulted. On the other hand, it is claimed that a consumptive who disposes properly of his sputum is not dangerous even to infants and children. The truth is, that it is very dangerous for an infant to remain in the same room with an actively tuberculous person, no matter how careful he may be. That a person who comes of tuberculous stock, when attacked by the disease, is apt to die in a short time is not true. On the contrary, such subjects are more apt to suffer from the chronic, mild type of the disease. Similarly, subjects who have suffered from scrofula, or tuberculosis of the glands, bones, and joints during childhood, seldom develop consumption. The belief that if tuberculosis was invariably detected in its incipient, nay in the "pretuberculous stage," all patients would be cured, has caused a considerable part of the distrust of the laity for the medical profession. It is impossible to detect the so-called pretuberculous stage, and in many cases it is more than difficult to detect active disease in its incipient stage. But even if we could diagnose all cases in their incipiency, i.e., as soon as the patient begins ailing, we should not save many more than we do at present. That it is not promptitude of diagnosis and the application of treatment which are always responsible for the cure of pulmonary tuberculosis, is clear when we bear in mind that autopsies show conclusively that more people recover from tuberculosis without treatment than suffer and perish from the disease. The fallacy that in order to diagnose incipient tuberculosis a physician must be a virtuoso in physical diagnosis is one of the causes why the disease is not diagnosed in time. A consideration first of the constitutional symptoms is more important. The signs only serve to localize the lesion. Between the ages of two and twelve years tuberculosis is almost always extrapulmonary. Such patients very rarely develop phthisis and are not a menace to other children since they do not disseminate bacilli. Such children should not be kept from school nor subjected to prolonged and costly treatment except such measures as will enhance their nutrition. The fear of pulmonary excavation is likewise without foundation, since cavities represent expectorated diseased tissue and are surrounded by

connective tissue capsules, preventing further extension. Remembering that over 50 per cent of patients suffering from pulmonary tuberculosis without treatment, are alive and more or less efficient at their occupations after five years from the onset of the disease, we can judge of the value of statistics as regards the efficacy of various cures for tuberculosis. Without the normal tendency of tuberculosis to heal, the sanatoriums may have to close their doors. We should also be on our guard against those remedies which are stated to work best in osseous, glandular, and articular tuberculosis. The prognosis in these cases is good as regards life.—*Traditional Fallacies About Tuberculosis, M. Fishberg, N. Y. Med. Jour., December 2, 1916.*

Classification of Tuberculosis.—The anatomic extent of the lesion is ignored in the proposed classification. The more important feature of the disease, namely, the constitutional or systemic disturbance, plays the chief part in the classification. This constitutional condition is accurately defined and measured by systematic record of the temperature and pulse rate. For the purpose of statistical records, W. divides cases of pulmonary tuberculosis into four groups; namely, those patients who, during a given period, are (*a*) fit for work and remain so; (*b*) fit for work, but become unfit; (*c*) unfit for work, but become fit for work; (*d*) unfit for work and remain so. He suggests that a useful comparative classification would be to combine this classification with an accurate measure of the constitutional condition as found in Inman's classification, and that it could be defined thus.

The condition of a patient suffering from pulmonary tuberculosis (that is, in whose sputum tubercle bacilli have been found) can be denoted at any given period during the course of the disease by one of the following combination of symbols: in_1 = resting febrile; in_2 = resting afebrile, ambulant febrile; in_3 = ambulant afebrile; A = fit for work and remaining so; B = fit for work, becoming unfit; C = unfit for work, becoming fit; D = unfit for work, remaining so.

The dividing line taken between febrile and afebrile is 99°F., the temperature being taken resting, not less than three-quarters of an hour after work.—*Classification of Cases of Pulmonary Tuberculosis, H. C. Wingfield, Brit. Jour. of Tuberc. October 10, No. 4, 1916.*

Tuberculosis and War.—The hardships and vicissitudes of the campaign are ample to explain the rousing of latent tubercular processes to an active destructive course, but probably direct recent contagion is responsible for a certain proportion of the morbidity. On the other hand, there are instances where the camp life seems to have given the finishing touch to the cure started under sanatorium or dispensary treatment, and the men are now found rugged and free from any signs of tuberculosis. Every province should make arrangements for one or more sanatoriums for tuberculous soldiers, and measures should be taken to make the soldiers take the needed courses of sanatorium treatment. The soldier has but one wish, and that is to return to his family, and the sick long for this even more than others. So it will be a difficult matter to get them to take proper sanatorium treatment. The military authorities may have to refuse to discharge the man from the army after the war until he has taken the required course of treatment. The sanatorium physician should be empowered to keep the man three or six months as his condition requires.—*Tuberculosi in guerra, A Fagiuoli, Gaz. degli Osp. e delle Clin., April 8, 1916.*

The Problem of the Tuberculous Soldier.—Nearly 300 men, the majority soldiers discharged from the army, have been admitted to this institution by arrangement with the insurance commissioners and the army authorities. Two main factors present themselves in dealing with the tuberculous soldier which are not present in the case of the soldier disabled, for example, by wounds. 1) The lesion is in many cases progressive, and the man's entire economic problem must be considered; 2) the factor of infection. The majority of these tuberculous soldiers regard their disease as something of comparatively little importance, and they are not disposed in many cases to submit to institutional discipline a moment longer than is necessary. Here again the economic position of the discharged tuberculous soldier becomes of supreme importance. From every point of view it would seem to be desirable not to discharge from the army the soldier suffering from tuberculosis until after an adequate course of treatment in hospital or sanatorium under military control. The case that is going down hill should be retained until the end. The patients in whom it has been found possible to "arrest" the disease should preferably be discharged, not directly to their homes but to undergo training in agricultural or horticultural work in farm colonies established for the purpose. The men would thus be trained to earn a living at that most difficult of things to come by for the "arrested" case—a suitable employment. The

points that this paper seeks to make are that this accommodation would be of much greater value and that the man himself and his dependents would be much better off if discharge from the army were deferred; also that sanatorium treatment should be followed by a further period of some months on a farm colony. Possibly after that many could be helped to take up small holdings and so remain "on the land."—*The Problem of the Tuberculous Soldier, E. H. R. Harries, The Lancet, December 2, 1916.*

Rarity of Tuberculosis in Workers in Lime.—Fisac has in various national and international congresses repeatedly drawn attention to the immunity against tuberculosis displayed by persons whose occupation brings them into close contact with lime and plaster. No one has impugned his statements in this line from 1905 to 1916, but no one has acted on the logical therapeutic conclusions therefrom, giving time to thoroughly modify the soil in treatment of tuberculosis, on a scale large enough to be conclusive. Each individual soil has its special chemical composition. How otherwise could a dog recognize its master by the sense of smell alone? This chemical composition decided whether tubercle bacilli can get a foothold and generate toxins in profusion or whether the tissues react with a fibrous growth, checking the proliferation of the germs. He quotes data tending to show that lungs and bones affected with tuberculosis have an abnormally low lime content. All the evidence to date is in favor of measures to render the soil more resistant, and he says that the compounds of lime take a leading position among such measures. He gives no technical nor clinical details here beyond these general statements.—*Rarity of Tuberculosis in Persons Working in Lime; Therapeutic Deductions (El terreno y la semillac), G. Fisac, Liglo Medico, November 11, 1916.*

Anti-Tuberculosis Movement in Massachusetts.—An account of the work accomplished in Massachusetts given before the Trudeau School of Tuberculosis, Saranac Lake, N. Y. B. refers to the early teachings of his father, the late Dr. Henry Ingersoll Bowditch, whose investigations as to the causative factors of pulmonary tuberculosis began in the early fifties. After eight years of study and research the elder Bowditch presented to the Massachusetts Medical Society a paper under the title, "Soil Moisture as a Cause of Consumption." This was in 1862. In 1885 Trudeau founded his famous institution, the first of its kind in America. In 1889, a small farm was purchased in Sharon, Mass., eighteen miles from Boston, and a building erected to accommodate eight women suffering from tuberculosis. This was done in accordance with the theory that this disease could be cured at a low altitude not far from the sea. In 1891 the Sharon Sanatorium opened its doors as a semi-charitable institution, the first of its kind in New England. B. traced the growth of tuberculosis work all through Massachusetts, as well as in some of our possessions, namely, the Philippines. He also refers to the types of treatment employed at the present time and concludes with a touching tribute to Edward Livingston Trudeau.—*The History of the Growth of the Anti-Tuberculosis Movement in Massachusetts, and the Lessons to be Learned Therefrom, Vincent Y. Bowditch, Boston Med. & Surg. Jour., December 14, 1916.*

The Syndrome of So-called Concealed Tuberculosis.—In a paper on this subject, Head of Minneapolis (Journal A. M. A., LXIII, 1914, page 996) ably discussed the problem of the relationship of concealed tuberculosis to many cases of so called tuberculosis; in a second paper (Am. Jour. of Med. Sciences, October, 1916), he presents the gist of his argument.

He makes a plea for the recognition of a clinical picture or symptom complex which he calls concealed tuberculosis. It occurs usually in persons under twenty-five years of age. A history of exposure to tuberculosis, even as far back as childhood, may be present. The symptoms consist of manifold manifestations of nervous and physical exhaustion, most patients presenting several of the following: indigestion, headache, constipation, mental depression, cold hands and feet, backache, neckache, asthenopia, voice tire, clearing of throat, crying spells, chilliness, loss of weight. As a rule these symptoms continue for a number of years, at times with periods of improvement, succeeded by relapses under unusual nervous and physical strain, frequently with partial or complete breakdown. The physician usually finds a poorly nourished and highly strung patient, whose features are angular, cheek bones high, chest and abdomen long, arms and legs slender, and reflexes active.

Carefully made and often repeated physical examinations will not disclose evidence of organic disease. Usually enteroptosis can be detected. The findings in the lungs are doubtful or negative. The rate of the pulse is generally increased, while the temperature is normal or shows an afternoon rise to 99.2° or 99.4° F. or higher. The laboratory findings, including the Wassermann test, are negative for organic disease, and

the Röntgen ray studies of the lungs for tuberculosis are doubtful or negative.

It is not astonishing, therefore, that a diagnosis of so called neurasthenia is made; but make a von Pirquet skin test and it will be promptly positive, and give a subcutaneous injection of tuberculin and it will always react positively. For this reason, Head argues, this symptom complex may be regarded as a special type of tuberculosis, without focal evidence, but discovered by a specific test. Head contends that most subjects who give the picture of nervous or physical exhaustion have physical disease of some sort, and that this will be unearthed if the examination is thorough; it may be tuberculosis, syphilis, ductless gland disorder, nephritis, or sepsis. In some of these patients, labelled neurasthenic, in whom examination fails to detect organic disease other than tuberculosis, the number of times in which a positive reaction to a maximum dose of tuberculin given subcutaneously will be obtained is astonishing and instructive. Head asserts that the number of negative reactions is small if the examination is careful and thorough and a large series is studied.

These cases are quite common and can be recognized by the specific tuberculin test. When properly diagnosed, they will be treated as tuberculous, which they are, and not as some form of nervous exhaustion, which they are not.

As to the exact site of the tuberculosis in the cases discussed here, no positive and final statement can be made. Sometimes the lesion is in the bronchial glands, sometimes at the hilum of the lungs, and in other cases in the mesenteric glands. In some there may even be some slight pulmonary involvement, either not sufficiently extensive or else too deeply placed to permit of detection by physical examination.—*Editorial N. Y. Med. Jour., November 11, 1916.*

What Constitutes Clinical Tuberculosis in Adults?—It is not only in the beginning cases of tuberculosis, that we err in our diagnosis, but just as much in the diagnosis of the moderately advanced and advanced cases. S. urges a consideration of the percentages of wrong diagnosis as cited by Ash and the fact that during only the past year a matter of 1.6 per cent of the individuals entering the State sanatoria of Massachusetts were either nontuberculous or not diagnosed. The responsibility is just as great in the diagnosis of the patient presenting with what seem to be all the necessary signs and symptoms for the diagnosis of advanced tuberculosis as in the doubtful case. The necessity of approaching the examination in these cases with a mind as free and unprejudiced by the history of cough or hemoptysis as is possible should be emphasized, remembering that almost any pathological condition in the pulmonary tract may simulate tuberculosis in every respect. Pottenger, in suggesting the consideration of the symptomatology from the etiological viewpoint, has made it easier to analyze the disease conditions. The essayist agrees with Lawrason Brown and others that the importance of physical examination in the diagnosis of pulmonary tuberculosis has been overemphasized in that symptoms are a better guide to activity than physical signs, and that symptoms without physical signs demand treatment, and physical signs without symptoms require only careful watching. It does not seem possible or probable that we can ever outline a symptom complex of certain signs and certain symptoms and say that these signs and symptoms in every case mean tuberculosis. It seems rather that we must value each symptom and each sign for itself and in conjunction with other symptoms and signs, for every case is a different one and has a different complex. Though deeming that certain outstanding symptoms, such as hemoptysis, cough, elevated temperature, increased pulse, and emaciation are suspicious of infection, we are not qualified to say that this is a case of active tuberculosis in an adult without proper and due consideration to other factors present.—*What Constitutes Clinical Tuberculosis in the Adult? G. L. Schadt, Boston Med. and Surg. Jour., August 31, 1916.*

Early Diagnosis.—In early tuberculosis, one of the most significant modifications of the respiratory murmur is what Turban calls "rough" breathing, in contradistinction to the smooth vesicular respiration. We may also have a diminution of the respiratory murmur on the affected side. The expiratory murmur may also be distinctly prolonged and may be more or less bronchial in character, the bronchvesicular murmur of Flint. "Cogwheel" respiration is of little value. After all, we must agree with Hector McKenzie that "the earliest physical sign which is really characteristic is the presence of râles." The râles may only be heard during the respiration following coughing. When heard only at the base, the cause must be other than tuberculosis. The symptoms, however, are to be relied upon chiefly. A diagnosis of active tuberculosis should never be made on the basis of an X-ray plate alone.—*The Early Diagnosis of Tuberculosis, Edw. O. Otis, N. Y. Med. Jour., October 21, 1916.*

Early Diagnosis of Pulmonary Tuberculosis.—The subject of early diagnosis of pulmonary consumption is becoming more and more complex. One sanatorium expert regards it as almost fatal to wait for bacteriological and stethoscopic signs and lays stress solely on pulse, evening fever, cough, and slight wasting, this syndrome often antedating the resources of physical diagnosis. A second expert takes the view that in many so-called incipient cases in which recovery occurs the patients never had tuberculosis, but have become objects of suspicion by sojourn in the sanatoria. There appears to be warrant for almost any extreme of opinion because of lack of standardization of diagnostic criteria. The discovery of bacilli in the sputum is still the only criterion, but since it is of limited prognostic value it must have backing of some sort. At present the Schrön-Much granules are the object of search of the bacteriologist, and if these are absent tuberculosis is regarded in some quarters as practically excluded. A great advance was made in this field when very small quantities of sputum were made to yield positive finds. The chance of finding bacilli varies directly with the amount of sputum available for repeated tests, and with the amount of time at the bacteriologist's disposal. From the latter viewpoint any method which can cut short the time without prejudice to thoroughness should be welcome to the clinician.

In Il Policlinico for July 9, Martelli publishes the following method for early recognition of bacilli in the sputum when expectoration is almost absent: 1. Give the patient up to one gram of iodide of potassium daily, with expectorants (senega, ipecac) for two or three days. 2. Collect from 100 to 200 cc. of sputum and treat it in the usual manner with antiformin in equal parts, leaving it from 2 to 4 hours in the thermostat. 3. Centrifugalize with high velocity, decant, and wash with saline solution, repeating this several times. 4. Make three very thin smears on slides, fix, and color with Giemsa stain in order to reveal ordinary bacteria, cell residues, etc. 5. Stain a slide with Ziehl's carbol-fuchsin with consecutive decoloration with acid and alcohol; another slide may be treated by Much's method, reserving a third one in case of failure of one or the other method, or of a double negative result. This technique may reveal the presence of a few isolated bacilli and of a few clusters of Schrön-Much granules and thus establish a diagnosis of incipient pulmonary tuberculosis. The author has been able to make this diagnosis in cases which clinically were regarded as examples of pretuberculous fever, Addison's disease, febrile anemia, chlorosis, etc.

Precisely the same technique may be used successfully in glandular tuberculosis by substituting borings from the glands for sputum.—*Editorial, Med. Record, Nov. 4, 1916.*

Diagnosis of Active Pulmonary Tuberculosis.—Report on six hundred tuberculosis suspects which were kept temporarily in a hospital to differentiate between those available for military duties and those deserving of release from such service. The diagnostic methods used comprised repeated physical examinations, radioscopy and radiography, bacteriological observations, the endermic tuberculin test, and systematic studies of the body weight, temperature, blood pressure, and pulse rate. Of the six hundred subjects eighty-nine were dismissed as non-tuberculous, having merely anemia, dyspepsia, emaciation, mitral lesions with hemoptysis, syphilis, pulmonary hydatid cysts, or nasal disorder. Eighty-three other cases showed tubercle bacilli in their sputa; in only thirty of these had the symptoms first appeared since the beginning of the war. The remaining 428 cases were labeled "suspects" and subjected to further observation. The essential X-ray evidence of tuberculosis in such instances was taken to be a veiled appearance of the lung —at the apex in two-thirds of all cases— generally with a more or less evident tracheobronchial adenopathy. The veiled condition, usually bilateral and varying greatly in density, did not permit of determining whether an existing tuberculous condition was active or in a cicatricial state. The conclusion was reached that actual lung tissue change predominates where there exist manifest dullness, exaggerated fremitus, crackling râles, hemoptysis, fixation of the apical veils, absence of change in these veils on coughing, and a striated or dotted condition. Pleural changes predominate where there are slight dullness, normal or diminished fremitus, and friction sounds, together with pupillary inequality and supraclavicular adenitis. The pleural type of apical shadow, different from the pulmonary type, permits some illumination of the apex to persist after coughing. Differentiation of active from healed lesions was accomplished, not by physical examination, but by general and functional observations on the patient, and by inquiry into his family history and the day of initial appearance of the disease. In doubtful cases, the iodide test was resorted to, one gram of potassium iodide being given on five successive days, and a rise in temperature of one half to one degree signified that the cicatrix

was not an old one. This test was applied, however, only where a favorable result was anticipated, the danger of lighting up a quiescent focus or inducing hemoptysis from a still active lesion being thus minimized. Of the 428 suspects, 216 were by these methods shown to be active cases and 212 healed cases. Adding to the latter the eighty-nine subjects classed as non-tuberculous, 301 out of the 600 soldiers examined were shown to be undeserving of relief from military service from the standpoint of tuberculosis—a not inconsiderable saving to the armed forces and finances of the nation.—*Les enseignements cliniques d'un Centre de triage de militaires suspects de tuberculose, E. Sergent and G. Delamare, Bull. de l'Acad. de Med., No. 43, October 31, 1916.*

The Hasty Diagnosis of Pulmonary Tuberculosis.—The problem of the early diagnosis of pulmonary tuberculosis is one upon which volumes have been written, and the general practitioner has received much criticism for his failure to diagnose the disease early enough to assure a permanent cure of the foci already present. We need not enlarge upon the great need to make such early diagnoses, nor upon the benefits to be derived. We are all agreed upon this fundamental point in the effort to eradicate tuberculosis. The next step is to diagnose the early cases, as demanded.

All in all, the diagnosis of pulmonary tuberculosis in an early stage is not easy, even for the expert in this field. Many cases are so puzzling in the early states, that, when confronted with them, even the expert finds himself in a state of indecision. What, then, shall we expect of the average physician, who has given but a moderate amount of time and energy to the problem, or, perhaps, has had no special training in this field?

One of the dangers in the effort to diagnose pulmonary tuberculosis as early as possible is that cases of a non-tuberculous nature may be labeled tuberculosis, with all that it means for the future welfare of the patient. Imagine diagnosing pulmonary tuberculosis in a patient who is really free from the disease in an active form, and his subsequent treatment as if he were afflicted with tuberculosis! Only one who has had the disease and made the sacrifices necessary to effect its early arrest can appreciate the full import of the wrongful diagnosis. This is perhaps especially true of a professional man who goes forth "to take the cure" in some far away resort or sanatorium, where he has no income, while his expense is by no means small; it may mean financial ruin. Financial ruin alone would not be so bad a result, if worse were not in store for a proportion of these persons. Some of them develop psychoneurotic states. Others become forever fearful of their health, and, in order to avoid possible overexpenditure of energy, limit their work so that they are never as fit and efficient as they were before. Still, others, become parasites upon their family, friends, or society. In fact, one in whom tuberculosis has been wrongly diagnosed is apt to have as many types of reaction as one who really has the disease. Furthermore, if the patient has some other disease which requires treatment of some sort beside the general hygienic, dietetic, rest and fresh-air treatment of tuberculosis, this too is neglected. The harm done may be irreparable.

Therefore, in spite of all that may be said in criticism of the practioner if he fails to diagnose pulmonary tuberculosis at an early stage when the evidence is sufficiently plain, he should not permit himself to label any case tuberculosis unless there is positive evidence that tuberculosis exists, and that this tuberculosis is active and not inactive, since inactive or old, healed tuberculosis should not lead to immediate treatment. Is not the modern view well expressed in the saying, *Jedermann hat am Ende ein bischen Tuberculose?* (Everyone has tuberculosis once in his life.)

When we are uncertain as to the diagnosis, we should be frank enough to admit our uncertainty. This means that we should keep all doubtful cases under observation long enough to permit thorough study. If, after a careful observation by all possible methods, including clinical history, temperature, physical examination, sputum examination, X-ray examination, and other methods of choice, we are unable to state positively that the patient before us has active pulmonary tuberculosis, we have no right so to label it. We can continue to keep the patient under observation, and, in the meantime, do all that is possible to improve his general health, regulate his habits, especially his hours of sleep, his hours of work, and his diet, with the addition of whatever individual hygienic measures we can employ.

Beware, the hasty diagnosis of pulmonary tuberculosis. It is an obligation that we owe our patients, society, and our own consciences.—*Editorial, N. Y. Med. Jour., October 7, 1916.*

Latent Tuberculosis.—Lymph nodes from a group of patients clinically free from tuberculosis were tested by inoculation into guinea-pigs for the presence of living tu-

bercle bacilli. The nodes were taken only from patients who had died and who showed no gross evidence of tuberculosis at autopsy. The nodes themselves, in every instance, were examined microscopically and found to be free from evidence of tubercle. A total of 32 cases were thus examined and the nodes from three were proved to contain living, pathogenic tubercle bacilli. A careful review of the literature showed that similar findings had been recorded by a few other workers, and when the results of all who had made such studies were included with those of the present series, they indicated that latent tuberculosis probably existed in an average of about 12 per cent of human beings. It was impossible to determine the duration of such latency in the human being, but some observations which have been made upon guinea-pigs showed definite latency for as long as 104 days.—*Latent Tuberculosis, C. Y. Wang, Lancet, September 2, 1916.*

Signs of Pleuritis at the Apex.—Sergent ascribes great importance to inflammatory processes in the pleura in the apex region, not only for the diagnosis of tuberlosis, but for distinguishing the form and the stage of the tuberculous process. This apical pleuritis is frequently accompanied by unequal pupils and enlargement of the supraclavicular glands. The pupil on the side affected is liable to be dilated or contracted, and the gland just back of the clavicle, at the external margin of the sternocleidomastoid, can be felt. When much enlarged it is soft, but otherwise hard. Sometimes it feels like a cord knotted along its course. This supraclavicular adenitis has nothing in common with cervical adenitis. It is connected with inflammation of the pleura in the apex region much more than with inflammation of the parenchyma at the apex. It is an objective, palpable sign of pleuritis at the apex. S. has found in cadavers a chain of lymphatics starting in the focus in the apical pleura and terminating in the supraclavicular ganglion palpated during life. When the ganglion is large and soft, the pleuritic process is probably active. When the pleural focus has long healed over, the gland shrivels and grows hard. This apical pleurisy is nothing new, but physicians seem to have forgotten it. The changes which it induces are liable to lead to the mistaken diagnosis of infiltration of the apex, when in reality there is only a benign lesion, a simple cicatrix, relics of a long past process.—*Semeiologic Importance of Signs of Pleurisy at the Apex. (Les signes de la pleurite du sommet et leur valeur dans le diagnostic de la tuberculose pulmonaire de l'adulte. L'adénite et la lymphangite nodulaire susclaviculaires.) E. Sergent, Presse Médicale, August 24, 1916, No. 47.*

Transmission of Sounds Through Pleural Effusions.—Viola's study of this subject has confirmed the fact that when whispered words can be auscultated the effusion is serious. When some of the letters seem to be dropped out of the words, the effusion is somewhat purulent. As less and less of the words is heard, but the bronchial murmur persists, the effusion is more and more purulent. When nothing can be heard, no decisive conclusions can be drawn. This sign known as Baccelli's phenomenon, assumes most importance after pectoriloquy of the whispered voice has reached its limit. —*Il fenomeno di Baccelli, G. Viola, Policlinco, September XXIII, No. 9.*

Diagnosis of Tuberculosis by Tuberculin.—A Study in Technique.—Ellis reviews the Calmette, Moro, and von Pirquet tests, and points out the objections to their general use. The failure of these methods to give entire satisfaction has led him to the adoption of a method which he describes and calls the papillary cutaneous method and the multi-papillary cutaneous method. This is done to distinguish it from von Pirquet's or the cutaneous method. The test is based on the fact that the papillary layer of the skin is the one influenced by tuberculin, and that it reacts to graduated doses, in definite proportion to the doses employed, with mathematical accuracy consistent with the character of the case. Usually six scarifications are made to which are applied graduated doses of tuberculin; there is also a control scarification. It has been found that the results are definitely proportional to the dose and the final reaction. There is a distinct connection between the multi-papillary cutaneous reaction and the class in which the case is, and this relation is sufficiently definite to be of great aid in diagnosis and prognosis. When the reactions do not agree, further investigation usually demonstrates the cause, for instance the lowering of the reaction by a previous course of tuberculin treatment. The results also indicate that the highest multi-papillary cutaneous reaction occurs comparatively early in the case; a greater subsequent extension of the disease gives a lower reaction. The writer believes he has sufficient evidence to justify the statement that the multi-papillary cutaneous test properly carried out materially facilitates the early recognition of active tuber-

culosis, is a material aid toward a general prognosis and a valuable indication in tuberculin treatment.—*The Diagnosis of Tuberculosis by Tuberculin. A Study in Technique, H. A. Ellis, Lancet, October 7, 1916.*

Complement Fixation in Tuberculosis.—The examination of 361 persons (25 of them normal, 11 questionably nontuberculous, and 325 definitely tuberculous), using both an emulsion and an autolysate prepared from living virulent human tubercle bacilli as antigens, shows that: (*a*) The complement fixation test for tuberculosis is not absolute, being positive only in about 30 per cent of all the clinically definite cases of tuberculosis, both active and inactive. Active cases give a higher percentage of positive results than inactive cases. (*b*) The value of the complement fixation test lies in the fact that, taken in conjunction with other findings, a definitely positive reaction makes the diagnosis of tuberculosis certain. (*c*) It is of value also from a differential diagnostic standpoint in that it indicates tuberculosis when positive, as against syphilis, carcinoma, abscess of the lung, empyema from other causes, bronchiectasis, etc. Corper points out that the practical absence of a reaction in nontuberculous cases makes this test, when positive, of far greater value in the diagnosis of tuberculosis than any of the biologic tests for tuberculosis thus far discovered. A positive test was never obtained in the absence of a positive von Pirquet reaction, but a large percentage of clinically normal individuals giving positive von Pirquet reactions were negative in fixation tests.—*Complement Fixation in Tuberculosis, H. J. Corper (Chicago), Jour. of Inf. Dis., September, 1916.*

Complement Fixation in Tuberculosis.—For a considerable time the results of this test in tuberculosis were irregular and unreliable, but enough was done to indicate that with proper improvements in methods the fixation reaction would become available for the diagnosis and clinical control of the disease. Other laboratory methods have served their purpose only to a limited extent. Almost all adults react positively to the skin reaction and the urochromogen test is equally unreliable, as well as the Arneth leukocyte count, albumin estimations of the sputum, agglutination reactions, etc. Granting that the circulating blood of tuberculous patients contains specific antibodies, the chief difficulty of all experimenters has been in the production of a suitable antigen. In previous communications Miller and Zinsser described a simple antigen prepared by grinding living or dead tubercle bacilli with dry table salt, and then adding distilled water up to isotonicity. This has served as an excellent antigen, and Miller reports the results of 1,000 cases tested with it. A table is given of the results, which are discussed. In the thousand cases there were 272 cases of active pulmonary disease, 113 cases of inactive pulmonary disease, 230 doubtful cases, 144 nontuberculous serums and 243 positive Wassermann serums. There were eight incipient cases without sputum, and few or vague pulmonary signs, which had been diagnosed in various ways among the 272 active pulmonary patients. Of the 213 inactive cases, the majority had been arrested for a period of years. Others had been diagnosed as inactive in a stage of clinical quiescence for a period of a few months. Summarizing, he finds that out of a total of 113 examined, 103 gave negative reactions, while ten showed fixation; 243 Wassermann serums gave negative reactions in all but seven. The following are the author's conclusions: (1) The reaction is practically always positive in active tuberculosis, 284 pulmonary cases; positive in 275, negative in nine; (2) Nontuberculous and normal patients react negatively; 144 cases; all negative. (3) The serums of syphilitics who have no clinically active tuberculosis are negative. Two hundred and forty-three positive Wassermann cases were all negative except seven, and in these seven tuberculosis was established in five cases and was not excluded in the other two. (4) The cutaneous and intracutaneous tuberculin tests and the complement fixation reaction are not identical or similar diagnostic procedures, since the former indicates the existence of a tuberculous lesion whether old and arrested or active, while the latter points clearly to the presence of some active focus. (6) There is evidence to believe that there exists a group of tubercle bacillus carriers who have no manifestations of clinical activity and whose serums contain no antibodies and yet discharge tubercle bacilli in their sputum. (7) The presence of tubercle bacilli in the sputum is not an absolute guarantee of the activity of the pulmonary tuberculosis. M. therefore feels justified in assuming that the complement fixation test with this antigen may be of distinct aid in the diagnosis of early and obscure pulmonary conditions. It should be valuable also in prognosis, as the reaction loses its intensity as the patient progresses toward recovery, and it gives the practitioner a measure for the control of tuberculosis in institutional and private life.—*Complement Fixation in Tuberculosis, H. R. Miller, Jour. A. M. A., November 18, 1916.*

Wassermann Reaction in Tuberculosis.—The Wassermann test was done on 290 tuberculous patients. Twenty-seven gave a positive reaction, of which 16 had a clear history of syphilis before admission, 5 admitted after admission to have had penile sores, 4 denied syphilis, but presented suspicious signs and histories, and 2 were doubtful cases. These 27 cases gave a doubtful plus reaction. Nineteen others gave one plus reaction. Of these, 8 gave a clear history of syphilis, 5 admitted sores and other symptoms of the disease and may be classed as syphilitics; 2 denied infection, but presented suspicious signs, and 4 were doubtful or negative cases. The percentage of plus reactions in the 290 cases is 15.6, of which 2 per cent may be classed as doubtful. Of the remaining 244 cases, 26 gave complement fixation with the cholesternized antigen and were negative with the non-cholesterinized antigen. Three of these were diagnosed as syphilitic, 3 as probably syphilitic, 10 as possibly but not probably so, and 10 frankly negative. Forty-seven other patients gave negative reactions with the non-cholesterinized antigen and almost or quite complete complement binding with cholesterinized antigen. Of these, 27 were considered frankly negative, 5 as positive, and 15 as doubtful latent. Of the 290 tuberculous patients 44 were classed as syphilitic (14.8 per cent), and 58 (20 per cent) as probably so.

Tuberculosis need not, in the absence of lues, give a positive reaction. The use of cholesterin in the antigen accounts for the number of positive reactions found in tuberculous patients free from syphilis. The number of non-syphilitic tuberculous patients whose blood may bind complement with non-cholesterinized antigen, is so small as to be negligible. Complete fixation with non-cholesterinized antigen is as much evidence of syphilis in a tuberculous individual as it is in a non-tuberculous one. The sera of non-syphilitic tuberculous patients will give partial to complete fixation of complement in 31 per cent of cases when cholesterinized antigen is employed.—*The Wassermann Reaction in Its Relation to Tuberculosis. Capt. C. G. Snow and Capt. Al. T. Cooper, Amer. Jour. of Med. Sciences, August, 1916.*

Contact Points Between Tuberculosis and Syphilis.—In order to test the supposition that a definite number of so-called tuberculous patients would be found to possess definite pulmonary syphilitic lesions, 471 patients in the Rutland Sanatorium, were given the Wassermann test. Of these, 430 were negative, 10 were doubtful, 2 were unsatisfactory, and 29, or 6 per cent were positive. Of the 430 negative cases, 140 had incipient pulmonary tuberculosis, 105 of these had repeated negative sputum, and 35 had positive sputum. Of the moderately advanced cases there were 222, and of these 75 had negative sputum and 149 had positive sputum. The remaining 68 were far advanced, and of these 7 were negative and 61 had positive sputum. The sputum was negative in four and positive in two of the doubtful cases in the incipient stage; two had negative and two positive sputum in the moderately advanced stage. There were no doubtful cases in the far advanced stage of their pulmonary disease. A positive Wassermann was obtained in 10 incipient cases, and of these 8 had negative sputum and 2 positive. In the moderately advanced stage, 4 had negative and 11 positive sputum. In the far advanced stage there were only 4 that gave a positive Wassermann, and in each instance the sputum was positive. From his experience the writer believes a careful inquiry should be made into all cases of pulmonary disease as to the possibility of a latent syphilitic infection, and if there is a suspicion of syphilis, the search should not be abandoned in a case of pulmonary disease with a positive or even a negative Wassermann without first having a careful radiograph taken of the lungs and the long bones. The presence of cavity signs in the lung and the expectoration of large amounts of sputum persistently negative to tubercle bacilli should always suggest pulmonary syphilis. If a positive reaction to tuberculin occurs in a given case of pulmonary disease with a marked positive Wassermann, it is difficult to make a correct diagnosis because the two diseases may coexist while the X-ray examination may not be of assistance.—*Contact Points Between Tuberculosis and Syphilis, James A. Lyon, Boston Med. and Surg. Jour., August 31, 1916.*

Tuberculosis or Syphilis of Lungs? A discussion of 8 cases which were eventually regarded as examples of pure syphilis. Other cases are quoted in which both diseases were associated. Patients with pure pulmonary lues may be admitted into tuberculosis sanatoria where they do not belong. A positive Wassermann reaction cannot exclude tuberculosis in such cases. Absence of tubercle bacilli in extensive pulmonary disease in association with syphilitic history or stigmata of that disease means that intensive syphilis therapy should be practised. Of great value in diagnosis is the presence or absence of fever. A patient

may have emaciation, night sweats, cough, and bloody sputum, but if he has no temperature syphilis should be suspected. Tuberculin as a diagnostic test is mentioned in but one case. These patients often do surprisingly well on potassium iodide. In cases of association of both diseases the presence of tubercle bacilli and positive Wassermann will often make the diagnosis, but in closed tuberculosis the bacillus may not be found. While the author has found a positive Wassermann in all of his mixed cases, others have not been so fortunate. He would place all subjects with tubercle bacilli and fever in the sanatoria and would keep all others out. He closes by quoting from a well-known syphilographer to the effect that in many cases an autopsy alone can explain the true mechanism, *i.e.*, to what extent is one disease determined by the other?—*Lungen-tuberculose oder Lungen-Syphilis?, Wilmans (Hamburg), Münch. Med. Woch., October 17, 1916.*

Tuberculosis and the Schools.—It is at school and by the school that society can root out tuberculosis. The physician has not only the right, but the duty to utilize the school, because it is here only that effectual prophylaxis can be applied. If there is no case of open tuberculosis in the environment, the infant may escape infection. Between three and five the lymphatic glands arrest any tubercle bacilli entering the organism. This localization in the glands may be the extent of the tuberculosis invasion. The child is not diseased, he is merely tuberculized, sensitized. The organism keeps on the defensive and gives a positive response to the tuberculin tests all through life, up to advanced age, testifying to a relative immunity. We can assume that practically every child is infected before it reaches fifteen. It is our task to distinguish between those who are holding their tubercle bacilli harmlessly imprisoned in their glands, and those whose bacilli are more active and flood the blood stream now and then with their toxins. The child does not develop normally, looks frail and the digestion is deranged, gastric anachlorhydria leading to intestinal trouble. These *tuberculisés évolutifs* are the candidates for phthis in later life.

Jeanneret emphasizes that tuberculosis in school children is always "closed." The children do not infect each other. They contract their disease in their homes or from the teacher. Every school child should have his health chart, the *fiche sanitaire*. On this should be recorded his weight every month and his height twice a year. The weight divided by the height gives a reliable index of the physiologic balance. The health chart should also record the tint of the mucous membranes, and whether the child is pale or ruddy, a good or bad student, and likewise any complaints or anomaly that may be noticed. The Pirquet skin test is indispensable. Once positive, it need not be repeated, but, if negative, it should be repeated once a year. With health cards like this, kept up to date, the children with evolving tuberculosis are automatically sifted out, and these require closer examination, including roentgenoscopy.

Jeanneret regards sunlight as the great regenerator in childhood. He has the children's gymnastic work done in the open sunlight, the children stripped to the waist. This idea of exercising with the upper part of the body exposed to the air has spread until now the Swiss soldiers systematically exercise in this way. He adds that gymnastic exercise for children from six to twelve should be predominantly thoracic. The child has special need of oxygen, and the only means to increase the supply of oxygen is by developing the respiratory function by gymnastic exercises of the chest. This develops the chest and lungs, keeps the costal articulations flexible, and thus materially reduces the predisposition to tuberculosis. Training of deaf-mutes in phonetic exercises has aided much in reducing the predisposition to tuberculosis in this group. Fully an hour in the course of the day should be devoted to gymnastic exercises in every school. He describes ten basic exercises.—*Tuberculosis and the Schools (Tuberculose et école), L. Jeanneret, Revue Méd. de la Suisse Rom., August, 1916.*

Infant Mortality in Families Where There is Tuberculosis.—Ustvedt has been compiling data in this line during the last five years at Christiania. When such a record has been continued for twenty years, tracing the later fate of the infants born in these families, unquestionably valuable lessons can be deduced from it. His material includes 480 infants, born in families where there was one or more members with tuberculosis in a contagious stage. An average of 19.2 per cent of the infants died within the first year of life while the average infant mortality in the city at large was 10.8 per cent. A number of tables are given for comparison of various data. They testify anew among other things to the dire influence of tuberculosis in the mother and of bottle feeding. Of the 19.2 per cent that died within the first year, 40 per cent had a

tuberculous mother, and of the 334 breast fed children only 10.5 per cent died while 28 per cent of the 128 bottle fed did not live through the first year. Only 37.1 per cent of the infants died of actual tuberculosis among the 124 that died during the five years in question. He comments that these figures teach nothing new, but they emphasize anew the vital importance of removing infants at once from tuberculosis in the environment, and especially from a tuberculous mother. Such statistical works as this can be utilized to educate the parents to the necessity for sending the infant out of the menacing environment. The tables show that when the mother had tuberculosis, the infant's danger was the greatest, whether it was bottle or breast fed.—*Spaedbarn i tuberkulose familier i Kristiania, Y. Ustvedt, Norsk Mágaz. f. Lacges videnckaben Oct., LXXVII, No. 10, 1916.*

The Tubercle Bacillus and the Child.—The exposure of the child to infection begins very soon after birth but whether a given inoculation will be overcome or not depends on the efficiency of its natural defenses. The skin offers an almost impenetrable barrier to germs and the main avenues by which they can invade are the nose and mouth, along with air, food and drink. They then come in contact with bactericidal secretions and a mucous membrane not easily penetrated when healthy. Arranged here and there also are masses of lymphoid tissue containing elements which have defensive properties and if they make their way beyond these the system is defended by the lymph and body cells, which are also defensive. While leukocytes possess protective properties to the highest degree, yet other cells are also more or less defensive. Pottenger calls attention particularly to the protective influence of the lymphatic system. The importance of the cervical glands in screening out and destroying bacteria can be readily appreciated and the enlargement of these glands is evidence of this. Tonsils and adenoids must often be removed, but they should be left untouched until the child has grown old enough to come in contact with pathogenic bacteria in sufficient numbers to have developed a specific immunity against them. There is danger at the present time for the tonsils on account of the discovery of their importance as a focus for streptococcal invasion, but there is no reason why their removal is necessary, at least early in life. He sums up his views in the following conclusions: 1. Immediately following birth the child is protected by a nonspecific cellular and humoral defense. 2. After coming in contact with tubercle bacilli, the fixed cells take on themselves a new property, that of producing specific protrolytic enzymes, whose function it is to destroy tubercle bacilli and their products. 3. The nonspecific defense is carried on largely by the lymphatic system, collections of lymphatic tissue, such as tonsils, adenoids and Peyer's patches being placed here and there where bacteria are likely to gain entrance to the tissues, so that bacteria may be taken up by them and destroyed. 4. When bacilli pass through the mucous membranes or these masses of lymphoid tissue, prior to the time that infection has occurred, they are carried directly to the lymphatic glands, in which they are destroyed or held captive. If they withstand the action of the lymph elements, they form a tuberculous focus. 5. Practically all tuberculosis, prior to the time that specific defense is created, is confined to the lymphatic glands; the exception being when large numbers of bacilli are taken into the body and find their way directly into the blood stream, by which they are scattered through the body, producing generalized tuberculosis. 6. After specific defense has been established, bacilli no longer pass readily through tissues, but are hindered by the fixed cells. A specific inflammatory reaction ensues, and the bacilli are either destroyed, or, if not destroyed, prevented temporarily, or wholly, from spreading. 7. This defensive inflammation results at times in a stimulation of fixed cells and increased fibrosis, producing encapsulation; at other times, necrosis followed by ulceration and the expulsion of the tuberculous mass. 8. The lymphatic structures are extremely important in their protective rôle prior to the time that specific cellular defense has been attained; consequently, tonsils and adenoids should be spared to the small child, unless indications for their removal are absolute. *The Nonspecific and the Specific Defense of the Child Against the Tubercle Bacillus, F. M. Pottenger, Jour. A. M. A., November 11, 1916.*